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KEY TO ABBREVIATIONS

c — correspondence
cr — case record
e — editorial

MMS — Massachusetts Medical Society
mp — medical progress
me — medical eponym

mr — meeting report
misc — miscellany
n — notice

o — obituary
* — original article

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NUMBER 1

CIVILIAN PUBLIC-HEALTH PROBLEMS IN WARTIME*

VLADO A. GETTING, M.D., DR.P.H.†

WORCESTER, MASSACHUSETTS

THE problem of civilian health is daily becoming more acute, although at present the health of the American people is as good as that of any other nation, if not better. This result has been achieved under peaceful conditions, but now we are at war. Here in Worcester, far removed from the battlefields and fighting, we are beginning to feel the pinch of war.

What are the problems of civilian health in Worcester? Is there going to be an increase in disease? Which diseases will become more prevalent? How can we safeguard the public health for the future? I propose to forecast the health status of the civilians in Worcester. We shall have an outbreak of some sort of illness, perhaps several, if the war lasts for years as is expected.

Perhaps we can best envisage the future of Worcester's health if we first review the occurrence of disease in previous wars. We can turn then to our experiences and review these in the light of war experience elsewhere.

MEDICAL HISTORY OF WARS

Former Wars

The history of wars prior to the twentieth century is characterized by accounts of great epidemics of bubonic plague, cholera, dysentery, malaria, smallpox, syphilis, typhoid fever and typhus fever. In twentieth-century warfare influenza, meningococcal meningitis and other respiratory diseases, venereal diseases and insect-borne diseases are the chief concern of military and civilian health authorities. Although the old-time diseases remain as possible dangers, they are controlled by continuous application of the principles of sanitation and epidemiology, and it is unlikely that they will again play a major role during war.

Under war conditions,¹ many of the safeguards of the health of both the military and civilian populations are abandoned. The crowding of large numbers of people in concentration camps, military establishments and air-raid shelters, or in an effort to keep warm, the primitive environmental sanitation and the lack of personal hygiene are all conducive to the spread of infectious diseases. The concentration and movement of armies and refugees, accompanied by the hardships of fatigue, general malnutrition and exposure and the lack of proper medical care provide the fuses for the explosion of widespread epidemics. More soldiers have been killed by infectious diseases than by bullets in all wars prior to the Franco-Prussian War of 1870, when the German Army experienced more deaths from battle than from disease. During the Russo-Japanese War of 1904, both sides suffered more from war casualties than from disease. In spite of the toll of influenza, the A.E.F. of 1917-1918 reported fewer deaths from sickness than from battle, although for the entire United States Army, at home and abroad, the deaths from disease were the more numerous of the two.

World War I

During and after World War I all infectious diseases except the common childhood communicable diseases were highly prevalent in eastern Europe.² There was an epidemic of typhus fever and relapsing fever throughout Russia, Poland and Serbia. Fortunately, these diseases did not spread into western Europe. Overshadowing all other outbreaks was the influenza pandemic, which caused an increased mortality from pneumonia. Meningococcal meningitis was epidemic, while dysentery, smallpox, tuberculosis and venereal diseases increased. Malaria, which had disappeared from most of Europe, returned to central, eastern and northern Europe to ravage the population.

*This and the two following papers were presented at a meeting of the Worcester District Medical Society, Worcester, September 9, 1942.
†Assistant in preventive medicine and epidemiology, Harvard Medical School and Harvard School of Public Health; commissioner of health, City of Worcester.

In the United States Army, respiratory diseases, venereal diseases, mumps, measles, dysentery and tuberculosis were the cause of about 95 per cent of absences from duty. Influenza, tuberculosis, measles and meningococcal meningitis were the leading causes of death. A most noteworthy fact is that the Army in the continental United States had generally higher rates for admission and days lost from duty on account of infectious diseases than did the A.E.F. Likewise, the Navy suffered a higher incidence of communicable diseases in training camps than on shipboard. The explanation of this phenomenon is that the Army and Navy personnel in this country were newly organized and therefore had a lower group resistance to infectious diseases; secondly, they were more exposed to infections from civilian populations than were the troops in Europe. Conversely, the danger of spread of infection from soldiers and sailors to civilians was enhanced in the United States.

World War II

In the present war, influenza, meningococcal meningitis and tuberculosis, as well as paratyphoid fever and bacillary dysentery, are again showing an increased incidence in the civilian population, both on the Continent and in the British Isles. Typhus fever and bacillary dysentery are of epidemic proportions in eastern Europe, and typhus will no doubt achieve high proportions during the coming winter. In Great Britain, the evacuation of school children did not result in an expected increase in the common communicable diseases, but, malnutrition, fatigue and lack of adequate shelter are the principal causes of the increase of illness in continental Europe. The hazards of infection have been intensified by crowding in bomb shelters. Scabies, impetigo and lice infestation are acute problems.

WORCESTER'S HEALTH PROBLEMS

As in modern warfare, so in the modern epidemiologic control of infectious diseases the maneuvers and strategy of the past do not offer a formula for success. Nevertheless an appreciation of former problems and of the experiences of the present war in Europe, together with the application of newer knowledge, may facilitate the control of infectious diseases in America. Undoubtedly the changed character of the leading infectious diseases of war and the partial limitation of outbreaks of classic war diseases may be considered the most encouraging results of the present-day epidemiologic control.

Industrial Accidents

The control of infectious diseases in Worcester is a joint responsibility of the medical profession

and the Health Department. Infectious diseases, however, are not the only problems with which we are faced today. With the increased rationing of food, which is apparently on its way, deficiency diseases of various types may become prevalent. With the employment of inexperienced laborers and of women, older men and the partially crippled in the war industries of the city, with overtime and the use of old machinery, unprotected by safeguards and with the crowding of machinery on a relatively small floor space in the rush of production, industrial accidents are bound to increase in number and severity. It is an accepted fact that crowded home conditions and worry and discomfort outside the workshop are responsible in large measure for many of the accidents that occur in industry. The roles of the physician, the health officer and the safety engineer are paramount. The United States Public Health Service³ has been most active in pointing out the hazards of industry and in developing methods for the conservation of the health of the war worker.

Malnutrition

Malnutrition has always been present in the United States.⁴ Surveys⁵ have revealed a surprisingly high incidence of nutritional deficiencies. The people of Worcester are better nourished than those in many parts of the country, but with rationing and food shortages, deficiencies are bound to occur. The employment in industry of both parents may result in nutritional disturbances among children. In an attempt to minimize malnutrition, the Worcester Health Department has secured the services of a nutritionist, lent to us by the Southern Worcester County Health Association.

Infectious Diseases

The control of infectious diseases is an ever-present problem. The health of the civilian population is vital and without it there cannot be victory. For some diseases we have adequate control measures, and the incidence of these has been steadily decreasing (Table 1).

Typhoid fever. Typhoid fever has decreased from a peak of 292 cases in 1909, when Worcester had a population under 150,000, to less than 10 cases a year since 1937. This decrease is due to proper control over water supplies, sewage disposal and food handling. Nearly all the recent cases are due to carriers or are secondary to unrecognized cases. We have had 7 cases in 1942. Three of these were in the same family; one was probably primary, with the other two patients secondarily infected. Three other cases occurred in a boardinghouse and were caused by a carrier who

helped prepare the food Unless there is a breakdown in our sanitation from bombing or because of mass evacuation, we do not expect any increase in typhoid fever

Other food borne diseases, however, may increase unless stricter measures are adopted in the sanitation of food handling establishments Small

four years Some of the decrease during the past ten years may be due to the experimental immunization conducted with the co operation of the Massachusetts Department of Public Health This program has now been abandoned owing to the unavailability of the immunizing material The last outbreak occurred in 1938 Since the incidence

TABLE 1 Incidence of Communicable Diseases in Worcester—1901–1941

PERIOD	AVERAGE POPULATION	DIPHTHERIA		SCARLET FEVER		TYPHOID FEVER	MEASLES		PULMONARY TUBERCULOSIS		WHOOPING COUGH	
		NO OF CASES	CASE RATE†	NO OF CASES	CASE RATE	NO OF CASES	NO OF CASES	CASE RATE	NO OF CASES	CASE RATE	NO OF CASES	CASE RATE
1901–1905	126 03	84	134	106	163	548	1578	257	1057	2 2		
1906–1910	144 341	3495	454	12 0	169	6 8	1 56	743	1696	234	2818	64
1911–1916	165 906	1815	271	1461	1 8	416	1 77	210	1715	191	341	41
1917–1920	184 657	1313	143	2031	7 0	198	93	81	1 16	185	510	55
1921–1925	183 743	177	182	2545	5	131	4 84	516	1077	117	1331	149
1926–1930	194 415	1038	10	2089	215	65	5 0	58	900	90	2 90	736
1931–1935	195 229	316	37	4113	4 1	54	315	344	52	77	2307	245
1936–1940	197 100	5	6	1844	197	20	515	87	697	2	31 5	331
1941	193 509	1	1	398	71	4	1318	681	124	64	3 8	195
1941*	193 509	1		41		4	1 4		3		1197	

*Figures are for the first six months

†All case rates are per 100 000 population

‡Made reportable in 1903

§Made reportable in 1907

food borne outbreaks have been frequent this year These are indications of things to come The Health Department is preparing regulations for the proper handling of food and the proper sanitation of food handling establishments

Diphtheria Diphtheria is another disease for which we have adequate control measures Immunization was started in Worcester in 1923 and the number of cases has rapidly dropped There has not been a death from diphtheria here for all most three years However, the disease has been increasing in Massachusetts during the past two years, and an outbreak, characterized by sporadic cases, is likely to occur

Every child over six months of age⁶ should be immunized with three doses of fluid toxoid at intervals of three weeks or two doses of alum precipitated toxoid at a month's interval One dose of the latter is not adequate⁷ Combined preparations of alum precipitated toxoid and Sauer's⁸ or Kendrick's⁹ whooping cough vaccine are available and are efficient Unless most of the children are immunized there may be a reappearance of diphtheria in epidemic form in Worcester and Worcester County The Health Department is re-immunizing with 0.5 cc of fluid toxoid all children through the first four grades who were immunized more than three years ago This procedure is based on studies¹⁰ which have demonstrated that there is a gradual loss of diphtheria antitoxin titer with time

Scarlet fever Scarlet fever has occurred in Worcester in irregular outbreaks every three or

four years Some of the decrease during the past ten years may be due to the experimental immunization conducted with the co operation of the Massachusetts Department of Public Health This program has now been abandoned owing to the unavailability of the immunizing material The last outbreak occurred in 1938 Since the incidence

of scarlet fever toward the end of 1941 was high, as it was at the beginning of 1942, and since the outbreaks are three or four years apart, we should be on our guard for an increase in scarlet fever during the coming winter, with a peak in the spring of 1943

Measles Measles is another disease in which we have no specific control measures Its cyclic outbreaks are more regular than those of the other communicable diseases Epidemics have occurred in Worcester almost every three years The last outbreak was in 1940 In 1941 measles was on the down grade, and this year we are apparently in the trough of the wave In 1943 we should therefore expect an epidemic of measles Sometimes these outbreaks may be delayed a year but either 1943 or 1944 will be marked by one

Tuberculosis Although tuberculosis has been rapidly decreasing, owing principally to the hospitalization of cases and the education of the public, an increase in this disease is probable So far in 1942 we have had an increased number of cases Many of these are among selectees who have been rejected because of possible pulmonary lesions These men are re-examined and re-examined If the diagnosis is confirmed the entire family is checked for possible disease Crowded living conditions long hours of work and malnutrition may result in an increased incidence of tuberculosis

Whooping cough At the present time we are experiencing a severe epidemic, but one that is not unduly alarming Unfortunately our control measures against this disease are not yet fully developed

We are experiencing a most unusual incidence of whooping cough, higher than at any time in the history of Worcester, and we have every reason to believe that this disease will continue in epidemic proportions for many months. Ordinarily whooping cough, like other respiratory diseases, has a peak in late winter and early spring. This year the disease has continued at an increased incidence during the summer. With the increase in respiratory diseases in the fall, it is to be expected that whooping cough will continue to be epidemic. Isolation of cases and quarantine of contacts are not adequate control measures. Children, especially infants over six months and under three years of age, can be immunized either by Sauer's or Kendrick's whooping cough vaccine. Other preparations have not proved effective in the experience of epidemiologists and are therefore not recommended. Immunization should be carried out as soon as possible, since immunity takes several months to develop. Inoculation after exposure is not effective.

Influenza. There is no statistical or epidemiologic basis on which a pandemic of influenza can be predicted. From all the evidence at hand, it is impossible to say whether there will be a worldwide pandemic during or following this war. But we have some comfort in the knowledge that if influenza does menace the world, the mortality, thanks to the sulfonamide drugs, will be much lower. Influenza is relatively mild; it is the complicating bacterial pneumonia that kills, and for this we are much better prepared than we were some twenty years ago. Antipneumococcus serums and the sulfonamides will save many lives.

Other diseases. Time does not permit an analysis of other diseases. I should, however, like to point out that meningococcal meningitis has been increasing in Massachusetts during the past two years, and that we may expect to see an outbreak of this disease characterized by sporadic cases widely distributed. The use of sulfonamide drugs and antimeningococcus serum will probably greatly decrease the fatality rate.

SUMMARY

In brief review, we can expect in Worcester and in Massachusetts an increase in diseases due to malnutrition and an increase in industrial accidents. There will in all probability be an outbreak of scarlet fever in Worcester during the coming winter, with a peak in the spring of 1943. Measles can be expected to reach epidemic proportions in the winter of 1943-1944. Pulmonary tuberculosis is increasing, and the longer the war lasts the greater will be the increase. At the present time we are experiencing a severe outbreak of whooping cough in Worcester. There is also an increase in diphtheria and meningococcal meningitis in Massachusetts; sporadic cases and minor local outbreaks of both these diseases are probable.

Typhoid fever will not increase unless there is a break in sanitation. Other food-borne diseases must be controlled by stricter measures. Physicians must co-operate in the control of all these diseases by keeping their patients at optimal health. This means regular physical examinations, correction of defects, good nutrition and adequate immunization of children against smallpox, diphtheria and whooping cough.

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HOSPITALS AND THE WAR*

CHARLES F. WILINSKY, MD†

BOSTON

MUCH has been said and a good deal written on the influence of the war on hospitals and hospital standards. In order that we may truly appreciate the significant roles which hospitals play in the life of a community, a brief picture of hospital evolution in the United States seems appropriate.

Hospitals, so aptly described as the workshops of the medical profession, have evolved in the comparatively short time of less than two thirds of a century from a total of approximately 150 hospitals with less than 30,000 beds to their present imposing size of over 6500 hospitals with more than 1,250,000 beds. Approximately \$4,000,000,000 represents the investment in the hospitals of America. More than 1,000,000 people are annually employed in these institutions, and over 12,000,000 people were hospitalized in the United States in 1941. What is the basic cause for this tremendous growth of the hospital system? The answer is found in the fact that the American public has increasingly recognized the advantages of the treatment of illness within hospital walls. Group judgment, availability of technical personnel, expensive and varied equipment including laboratories, x-ray units and so forth, all play their part in accurate diagnosis and scientific care. The average hospital stay has been tremendously shortened, the duration of illness lessened, and the wage earner restored to his job at an earlier moment, this representing an economic benefit of inestimable importance to the individual and the community.

As medicine has progressed, hospitals have contributed to its development in many ways. Normally the hospital concerns itself with the care of the patient, the training of personnel, the furtherance in varying degree of medical research and the teaching of people for more healthful living. To these fundamental services the war has added additional responsibilities. These include facilities in the event of enemy penetration, for the protection of patients, personnel and plant, the care of the injured and the evacuation of patients. These normal as well as abnormal functions represent a staggering load which is complicated materially at present by the enormous and constantly increasing shortage of personnel.

The personnel includes both the professional and the nonprofessional groups. Among the former are physicians, including interns and residents, nurses, laboratory personnel, dietitians, pharmacists and so forth. In the latter group are included everyone engaged in what we term the nonprofessional activities. Hospitals cannot compete with private industry. Many hospitals are dependent on private philanthropy, in order that essential free services may be rendered to those unable to meet the cost of hospital care. Industry is logically organized for profit. Hospitals, therefore, must normally employ those willing to work for what may be termed the lesser wage. The great demand in industry for labor, in all its forms, has depleted the hospitals of clerical workers, maids, waitresses, porters, scrubwomen, laundry workers, maintenance men and others and has indeed imposed great hardships on them.

Mention must also be made of the rising cost of supplies, as well as their quite frequent scarcity.

What are we going to do about it? This is a challenge that must be met. Hospitals must continue to function, and hospital care must continue to be given. We must not lower the standards, which are important for the preservation of life. We must continue to provide essential equipment and supplies. Judgment in its keenest form, however, will have to be exercised. The use of substitutes and relatively simple methods and procedures will be justified when the patients' welfare is not sacrificed. The critically ill must have priority and there must be a rationing, so to speak, of doctors, patients and hospital beds when that appears necessary.

We must curtail whenever possible. As an example, the laboratory and the x-ray should be limited to essential needs, and not used with the repetitious freedom of the past. Volunteers must supplement the efforts of the diminished ranks of paid personnel. The public must become educated to be less exacting, less demanding, more patient and more tolerant. They must be educated, for example, to go to their physicians for check ups and to hospitals only for the type of illness requiring hospitalization. They must be educated to require special nursing only when truly indicated, and to leave the depleted nursing personnel for the seriously ill. We must teach them to realize that everything is being done and will be done for their necessary care. Impatience with nurses

*An abstract of a paper presented at a meeting of the Worcester District Medical Society, Worcester, September 9, 1947.

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We are experiencing a most unusual incidence of whooping cough, higher than at any time in the history of Worcester, and we have every reason to believe that this disease will continue in epidemic proportions for many months. Ordinarily whooping cough, like other respiratory diseases, has a peak in late winter and early spring. This year the disease has continued at an increased incidence during the summer. With the increase in respiratory diseases in the fall, it is to be expected that whooping cough will continue to be epidemic. Isolation of cases and quarantine of contacts are not adequate control measures. Children, especially infants over six months and under three years of age, can be immunized either by Sauer's or Kendrick's whooping cough vaccine. Other preparations have not proved effective in the experience of epidemiologists and are therefore not recommended. Immunization should be carried out as soon as possible, since immunity takes several months to develop. Inoculation after exposure is not effective.

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SUMMARY

In brief review, we can expect in Worcester and in Massachusetts an increase in diseases due to malnutrition and an increase in industrial accidents. There will in all probability be an outbreak of scarlet fever in Worcester during the coming winter, with a peak in the spring of 1943. Measles can be expected to reach epidemic proportions in the winter of 1943-1944. Pulmonary tuberculosis is increasing, and the longer the war lasts the greater will be the increase. At the present time we are experiencing a severe outbreak of whooping cough in Worcester. There is also an increase in diphtheria and meningococcal meningitis in Massachusetts; sporadic cases and minor local outbreaks of both these diseases are probable.

Typhoid fever will not increase unless there is a break in sanitation. Other food-borne diseases must be controlled by stricter measures. Physicians must co-operate in the control of all these diseases by keeping their patients at optimal health. This means regular physical examinations, correction of defects, good nutrition and adequate immunization of children against smallpox, diphtheria and whooping cough.

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voted entirely to medicine; they carry on the hospital medical services and do consultant work. Their work will be further increased by a shortage of interns and hospital residents, and they will be required to spend more time in the hospitals. The number of surgeons will surely be depleted. All the specialties will have their problems, and the specialists will be so busy they cannot be expected to do other than their own work except in an emergency.

The chief problem we must meet is that of furnishing general medical care—the routine office work and housework. Of the 67 physicians in general practice, 8 are older men and of limited physical capacity. Of the group of surgeons, 8 do considerable general work, as do 5 obstetricians, giving, with the 20 internists, 92 men to do general medical work for 200,000 people. We can expect that the number will be further depleted by military service, illness and other factors, and furthermore, we shall not have the annual supply of young men starting to practice in Worcester.

Approximately 50 per cent of the house calls were made by men in the group that has gone into military service. These figures indicate a shortage of medical service quantitatively analogous to the shortage of gasoline. The question arises what can be done about it. One obvious answer is to let each physician handle his own problem in his own way and hope for the best. The other solution is some sort of co-operative planning. If the supply of gasoline were substantially limited as it is, and it were left to each dealer to use his own judgment in distributing his supply, we should undoubtedly have great confusion, inequalities and public resentment and a demand for government intervention. The medical profession faces similar hazards. Medical service, however, cannot be rationed by coupons. We have to take care of the sick, we have to man our hospitals.

What can be done by doctors as a group, is a problem for our society to decide. The specialists can organize themselves and handle their own peculiar problems. For the problem of general medical care during the emergency, we should have some sort of study committee to make definite suggestions concerning how we can best use our resources and keep in constant touch with the medical situation.

We must have public co-operation. To do this we must have definite recommendations to make to the public that will be helpful and not confusing. Many suggestions have been made. It is obvious that the doctor's time must be conserved and house calls be kept at a minimum. The doctor's day is planned in the morning, and when

possible house calls should all be received by 8 a.m. Vague directions such as "Do not call the doctor except when necessary" are useless, but if we could give the public a few concise statements of symptoms that are urgent and of those that are not, it might be helpful. For instance, abdominal pain lasting more than a few hours is urgent. Pain in the chest and bloody sputum are important, as is abnormal bloody discharge from any part of the body. On the other hand, a head cold with general malaise is not an emergency. We might in a tactful way explain to the public that chronic symptoms, nervousness, fatigue and so forth should be investigated, but that this should be done at the convenience of the physician. The periodic health examination, desirable as it is, may have to be postponed. As a substitute for it we might urge prompt examination at the appearance of new symptoms.

Many persons working in industry are on shifts that make it impossible to see the physician in his regular office hours, and must often do so in the morning. Many practitioners spend a good part of their mornings in the hospitals, and it would be a convenience and timesaver if facilities could be furnished for doctors to receive private patients at the hospitals when necessary. Some physicians find it necessary to see office patients by appointment, and we might obtain public co-operation in this. On the other hand, these physicians will probably have to examine urgent cases between or after appointments.

The greatest problem will be to cover house calls, especially calls at odd hours, at night and in emergencies. Nothing will be more discouraging or panicky to the public than calling one doctor after another unsuccessfully, and nothing will do more to create a public demand for government intervention in medical practice. We should have some definite plan to present to the public for this situation.

Probably the best plan would be a medical bureau maintained by our society to handle such calls at all times. However, the expense and organization involved make this impractical. An alternative plan might be this: Our hospitals have experienced switchboard operators available day and night. If we could obtain the co-operation of the hospitals, we might have each hospital act as a center to cover emergency calls. There could be kept at each switchboard a list of physicians available for such calls, including not only members of the staff, but physicians in the neighborhood without hospital affiliations. The public could then be instructed that if they cannot obtain a doctor of their choice they are to call the nearest hospital, and that the operator will then

undertake to send a physician. When the operator obtained a physician she would check his name on the list so that he would not be called again until the rest of the list was covered. If she failed to obtain a doctor in a real emergency, she could offer to send a cab, or if necessary an ambulance, to bring the patient to the hospital for emergency treatment. Thus the inevitable criticism of a neglected emergency could be avoided. This list of physicians would be kept available to the doctors so that everyone would be encouraged to do his share. In this way the hospitals could do a considerable public service without undue inconvenience or expense.

Our facilities will be strained to the utmost this winter during the usual epidemic of respiratory infections. One of our members suggested that we might obtain the co-operation of the district and public-health nurses so that at the request of a physician a nurse might visit a patient and give a report of the temperature, pulse and respirations and the appearance of the throat and general symptoms, and administer simple treatment at the physician's direction. This, of course, would have to be followed up either by a visit of the physician or by a satisfactory progress report by the nurse.

In this emergency the physician must conserve his own health and strength. It has been repeatedly shown in industry that fatigue is a leading cause of illness and accident, and no doubt fatigue makes the physician less effective and more liable to make mistakes. Every time a physician falls ill, the whole situation is aggravated. This means that physicians must have adequate rest and an occasional holiday.

* * *

In summary, we are faced with the problem of furnishing adequate medical service to the hospitals, industries and civilian populations of our communities in spite of greatly reduced personnel. In doing this we aim to preserve the high standards and best traditions of medical practice, and to do it so well that there will be no public demand for government intervention.

In order to accomplish this purpose, co-operative effort will be necessary, and we shall have to make the fullest use of our hospital facilities and the nursing profession. Every physician in civilian practice is as obligated to do his part as is the physician in the armed forces to fulfill his duties.

390 Main Street

THE RELATION OF SEASON, WEIGHT AND PRICE TO THE VITAMIN C CONTENT OF ORANGES*

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ORANGES, principally in the form of juice, are extensively used by persons of all ages. Children, particularly infants, whose dietary usually lacks variety, are given orange juice as a source of vitamin C to prevent scurvy, and probably a large proportion of adults also ingest it, principally for its vitamin C content. It is impossible to determine accurately the amount of orange juice consumed in this country per year as an intentional source of vitamin C, but it is reported that the value of the 1941-1942 orange crop is in excess of \$117,000,000.¹ It has been estimated that oranges contribute about 624,080,000 gm. of vitamin C to the human dietary annually.² Thus they constitute one of the most important natural sources of this vitamin. In fact, if one assumes that the average daily requirement of vitamin C by 130,000,000 people in the United States is 75 mg. per person,

the orange crop would supply 17.5 per cent of the needed supply.² This being so, information concerning the vitamin C content of oranges is of definite interest to physicians, nutritionists and others responsible for the human dietary.

As shown in a study by Holmes, Pigott and Tripp,³ the vitamin C content of oranges purchased in this locality varied over wide limits and bore no close, consistent relation to the brand or the section of the country in which the fruit was grown. These results naturally prompted the present study of the relation of season, weight and cost to the vitamin C content of oranges purchased under normal trade conditions in this country.

SOURCE AND TYPE OF FRUIT

The oranges used in our study were purchased at a number of local retail stores, some of which were members of large chain-store organizations and some of which were under private-grocery-store management. Some purchases were also

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made from street-side hucksters. The oranges were purchased on a per-dozen basis, since it was assumed that the average family of urban and nearby suburban localities would presumably purchase in this quantity. An attempt was made to select fully ripe, plump, juicy fruit such as would be selected by the average thrifty buyer. Since oranges available in this locality are principally grown in California and Florida, an attempt was made to purchase approximately an equal number of samples of oranges from each of these localities. Unfortunately it was not possible to accomplish this at certain seasons of the year.

PROCEDURE

The oranges were assayed for their vitamin C content by the indophenoluraturation method. The juice was expressed from the fruit with a glass reamer. It was then strained through a light cotton 14 mesh strainer to remove the seeds and pulp. Care was exercised that the juice did not come in contact with metal at any time and that it did not remain exposed to the air after it was removed from the fruit.

The vitamin C determinations were made by combining 2 cc. of the strained juice with 20 cc. of 8 per cent acetic acid in a 50 cc Erlenmeyer flask. This mixture was titrated with the dye solution, which was added from a microburette until the final drop produced a faint pink end point that remained for at least thirty seconds. The dye solution was prepared by dissolving 0.1 gm. of sodium 2,6-dichlorobenzenoneindophenol in hot distilled water, made up to a volume of 200 cc and standardized against a solution containing 0.1 gm. of vitamin C (Cebione, Merck) in 100 cc of 8 per cent acetic acid, according to the method of Tripp, Satterfield and Holmes.¹

EXPERIMENTAL DATA

In order that the data accumulated in this study may have direct practical value to the reader, they are discussed in terms of daily human vitamin C requirements. Even a cursory survey of the literature reveals considerable disagreement regarding these requirements, but in the past it was generally accepted that 25 mg.⁷ or 30 mg.⁸ constitutes the minimal optimum requirement. Olliver,⁷ Hawley⁸ and Sweany et al.⁹ believe that 50 mg. represents the desired daily consumption. On the other hand, the American Medical Association (Smith¹⁰) holds that 50 mg. should probably be considered as the barely adequate rather than the optimal requirement, with considerably larger quantities desirable when economically possible. Van Eekelen,¹¹ Heinemann¹² and Sweany et al.⁹ recommend 60 mg. for the average adult, with larger quantities

for pregnant and lactating women. The requirements in pathologic conditions such as tuberculosis, nutritional anemia, scurvy, myeloid leukemia and Addison's disease may be many times that of the average normal young adult. For instance, Martin and Heise¹³ and Trautwein¹⁴ recommend from 150 to 200 mg. daily in the treatment of severe tuberculosis; Heilmeyer¹⁵ found that the daily administration of 300 to 600 mg. enhanced the therapeutic activity of iron in the treatment of secondary anemia; Abt and Farmer¹⁶ secured considerable depigmentation in Addison's disease by the oral administration of 450 mg. of vitamin C daily; Bastedo¹⁷ comments on the treatment of severe scurvy with 1500 mg. and Eufinger and Giechtgens¹⁸ restored to normal a patient with myeloid leukemia by the administration of 2000 mg. Although the population of the United States includes both normal persons and those suffering from various pathologic conditions, it has been assumed in this study that the recommendation of the Committee on Food and Nutrition of the National Research Council¹⁹ of 75 mg. per day constitutes a suitable human adult requirement.

Data concerning the influence of seasons on the vitamin C content of oranges were obtained by purchasing representative fruit in local retail markets in March, June, September and December, it was thought that this procedure was typical of orange purchases in this locality during the spring, summer, fall and winter seasons. An attempt was made at each season to secure representative fruit of different sizes, price levels and brands.

Table 1 contains data relative to the season, source, weight, cost and amount of juice per orange. It also reports the vitamin C content per 100 cc. of juice, the amount of juice required to produce 75 mg. of vitamin C and the cost of this amount on the basis of each orange assayed, except that the March assays were made on the composite juice of two to four oranges. For convenience in comparing the size of the orange with the other data, the samples have been arranged for each season in order of increasing weight.

The results obtained for the oranges assayed in March vary over wide limits and show average per-orange values of weight 206 gm., cost 28 cents per dozen, 77 cc. of juice, 52 mg. of vitamin C per 100 cc. of juice, and 144 cc. of juice required to yield 75 mg. of vitamin C at a cost of 48 cents. Similar values for June were 150 gm., 29 cents, 74 cc. of juice, 45 mg. of vitamin C, and 176 cc. of juice at a cost of 59 cents. In September the values were 160 gm., 27 cents, 76 cc. of juice, 39 mg. of vitamin C, and 196 cc. of juice at a cost of 59

undertake to send a physician. When the operator obtained a physician she would check his name on the list so that he would not be called again until the rest of the list was covered. If she failed to obtain a doctor in a real emergency, she could offer to send a cab, or if necessary an ambulance, to bring the patient to the hospital for emergency treatment. Thus the inevitable criticism of a neglected emergency could be avoided. This list of physicians would be kept available to the doctors so that everyone would be encouraged to do his share. In this way the hospitals could do a considerable public service without undue inconvenience or expense.

Our facilities will be strained to the utmost this winter during the usual epidemic of respiratory infections. One of our members suggested that we might obtain the co-operation of the district and public-health nurses so that at the request of a physician a nurse might visit a patient and give a report of the temperature, pulse and respirations and the appearance of the throat and general symptoms, and administer simple treatment at the physician's direction. This, of course, would have to be followed up either by a visit of the physician or by a satisfactory progress report by the nurse.

In this emergency the physician must conserve his own health and strength. It has been repeatedly shown in industry that fatigue is a leading cause of illness and accident, and no doubt fatigue makes the physician less effective and more liable to make mistakes. Every time a physician falls ill, the whole situation is aggravated. This means that physicians must have adequate rest and an occasional holiday.

* * *

In summary, we are faced with the problem of furnishing adequate medical service to the hospitals, industries and civilian populations of our communities in spite of greatly reduced personnel. In doing this we aim to preserve the high standards and best traditions of medical practice, and to do it so well that there will be no public demand for government intervention.

In order to accomplish this purpose, co-operative effort will be necessary, and we shall have to make the fullest use of our hospital facilities and the nursing profession. Every physician in civilian practice is as obligated to do his part as is the physician in the armed forces to fulfill his duties.

390 Main Street

THE RELATION OF SEASON, WEIGHT AND PRICE TO THE VITAMIN C CONTENT OF ORANGES*

ARTHUR D. HOLMES, PH.D.,† JAMES A. PATCH, S.B.,‡ AND FRANCIS TRIPP, M.S.‡

STONEHAM, MASSACHUSETTS

ORANGES, principally in the form of juice, are extensively used by persons of all ages. Children, particularly infants, whose dietary usually lacks variety, are given orange juice as a source of vitamin C to prevent scurvy, and probably a large proportion of adults also ingest it, principally for its vitamin C content. It is impossible to determine accurately the amount of orange juice consumed in this country per year as an intentional source of vitamin C, but it is reported that the value of the 1941-1942 orange crop is in excess of \$117,000,000.¹ It has been estimated that oranges contribute about 624,080,000 gm. of vitamin C to the human dietary annually.² Thus they constitute one of the most important natural sources of this vitamin. In fact, if one assumes that the average daily requirement of vitamin C by 130,000,000 people in the United States is 75 mg. per person,

the orange crop would supply 17.5 per cent of the needed supply.² This being so, information concerning the vitamin C content of oranges is of definite interest to physicians, nutritionists and others responsible for the human dietary.

As shown in a study by Holmes, Pigott and Tripp,³ the vitamin C content of oranges purchased in this locality varied over wide limits and bore no close, consistent relation to the brand or the section of the country in which the fruit was grown. These results naturally prompted the present study of the relation of season, weight and cost to the vitamin C content of oranges purchased under normal trade conditions in this country.

SOURCE AND TYPE OF FRUIT

The oranges used in our study were purchased at a number of local retail stores, some of which were members of large chain-store organizations and some of which were under private-grocery-store management. Some purchases were also

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†Formerly, director of research, E. L. Patch Company; now, research professor of chemistry, Massachusetts State College, Amherst.

‡Research chemist, E. L. Patch Company.

made from street-side hucksters. The oranges were purchased on a per-dozen basis, since it was assumed that the average family of urban and nearby suburban localities would presumably purchase in this quantity. An attempt was made to select fully ripe, plump, juicy fruit such as would be selected by the average thrifty buyer. Since oranges available in this locality are principally grown in California and Florida, an attempt was made to purchase approximately an equal number of samples of oranges from each of these localities. Unfortunately it was not possible to accomplish this at certain seasons of the year.

PROCEDURE

The oranges were assayed for their vitamin C content by the indophenoltitration method. The juice was expressed from the fruit with a glass reamer. It was then strained through a light cotton 14-mesh strainer to remove the seeds and pulp. Care was exercised that the juice did not come in contact with metal at any time and that it did not remain exposed to the air after it was removed from the fruit.

The vitamin C determinations were made by combining 2 cc. of the strained juice with 20 cc. of 8 per cent acetic acid in a 50-cc. Erlenmeyer flask. This mixture was titrated with the dye solution, which was added from a microburette until the final drop produced a faint-pink end point that remained for at least thirty seconds. The dye solution was prepared by dissolving 0.1 gm. of sodium 2,6-dichlorobenzeneindophenol in hot distilled water, made up to a volume of 200 cc. and standardized against a solution containing 0.1 gm. of vitamin C (Cebione, Merck) in 100 cc. of 8 per cent acetic acid, according to the method of Tripp, Satterfield and Holmes.⁴

EXPERIMENTAL DATA

In order that the data accumulated in this study may have direct practical value to the reader, they are discussed in terms of daily human vitamin C requirements. Even a cursory survey of the literature reveals considerable disagreement regarding these requirements, but in the past it was generally accepted that 25 mg.⁶ or 30 mg.⁸ constitutes the minimal optimum requirement. Olliver,⁷ Hawley⁸ and Sweany et al.⁹ believe that 50 mg. represents the desired daily consumption. On the other hand, the American Medical Association (Smith¹⁰) holds that 50 mg. should probably be considered as the barely adequate rather than the optimal requirement, with considerably larger quantities desirable when economically possible. Van Eekelen,¹¹ Heinemann¹² and Sweany et al.⁹ recommend 60 mg. for the average adult, with larger quantities

for pregnant and lactating women. The requirements in pathologic conditions such as tuberculosis, nutritional anemia, scurvy, myeloid leukemia and Addison's disease may be many times that of the average normal young adult. For instance, Martin and Heise¹³ and Trautwein¹⁴ recommend from 150 to 200 mg. daily in the treatment of severe tuberculosis; Heilmeyer¹⁵ found that the daily administration of 300 to 600 mg. enhanced the therapeutic activity of iron in the treatment of secondary anemia; Abt and Farmer¹⁶ secured considerable depigmentation in Addison's disease by the oral administration of 450 mg. of vitamin C daily; Bastedo¹⁷ comments on the treatment of severe scurvy with 1500 mg., and Eufinger and Gaehgens¹⁸ restored to normal a patient with myeloid leukemia by the administration of 2000 mg. Although the population of the United States includes both normal persons and those suffering from various pathologic conditions, it has been assumed in this study that the recommendation of the Committee on Food and Nutrition of the National Research Council¹⁹ of 75 mg. per day constitutes a suitable human adult requirement.

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HEMORRHAGE FROM MECKEL'S DIVERTICULUM IN AN ADULT

Report of a Case

ABRAHAM SERVETNICK, M.D.* AND HOWARD G. NICHOLS, M.D.†

HAVERHILL, MASSACHUSETTS

MECKEL'S diverticulum occurs as a result of failure or complete obliteration of the omphalomesenteric duct. Its structure depends on the degree of obliteration that has taken place. It is usually situated on the antimesenteric side of the ileum, 30 to 90 cm. proximal to the ileocecal valve, but in rare cases it may occur at any other point in the gastrointestinal tract.¹ The tip of the diverticulum often lies free in the abdominal cavity. It may be attached to other viscera or to the abdominal wall, and rarely may be situated between the leaves of the mesentery.² Most diverticula are not over 10 cm. in length, but Tisdall³ has reported a diverticulum which was more than 100 cm. long.

Meckel's diverticulum occurs twice as often in males as in females,^{4, 5} and pathologic lesions involving it occur with greatest frequency in early childhood, but may do so at any age. The presence of a Meckel's diverticulum in approximately 2 per cent of the population^{1, 2, 6} and the fact that every third or fourth diverticulum becomes the seat of disease^{1, 4} emphasize the importance of this appendage in the differential diagnosis of abdominal disease.

Ulceration with hemorrhage or perforation; acute inflammation, various forms of obstruction and neoplasms are the important lesions with which this structure may be affected. Obstruction and inflammation are the pathologic entities most frequently encountered in adults, whereas hemorrhage is by far the commonest lesion in children.⁷

The presence of heterotopic tissue, which has been estimated to occur in 25 per cent of these diverticula,⁸ is significant, for it renders the latter particularly susceptible to ulceration. Gastric and jejunal mucosa and pancreatic tissue are the usual types of aberrant tissue found. Hudson and Koplik⁹ found gastric mucosa in 50 per cent of 23 cases of Meckel's diverticulum. Johnston and Renner¹⁰ reviewed 78 cases and found heterotopic tissue in 64, of which 50 presented evidence of ulceration. Moreover, intestinal hemorrhage occurred in 75 per cent of the cases containing the heterotopic cells. On the other hand, Brown and Pemberton¹¹ in 47 cases in which the diverticulum had been surgically removed, noted that bleeding had not occurred in any case and that the diverticulum contained gastric tissue in only 8 cases.

These studies suggest that the presence of gastric mucosa in a Meckel's diverticulum is deleterious and increases the likelihood of dangerous complications; for ulceration, when it does occur, usually develops at the junction of the ileal and heterotopic gastric mucosa, forming a marginal ulcer akin to a gastrojejunal ulcer. The ulcer is apparently the result of erosion of the intestinal mucosa by the secretions of the heterotopic gastric cells.¹⁰ The ulcer so formed usually penetrates the wall for a considerable depth. The variation in the site and extent of these ulcerations is dependent on whether only a part or the whole of the diverticulum is lined with gastric mucosa. The majority of the ulcers are situated at the bases of the diverticula. The accompanying diagram

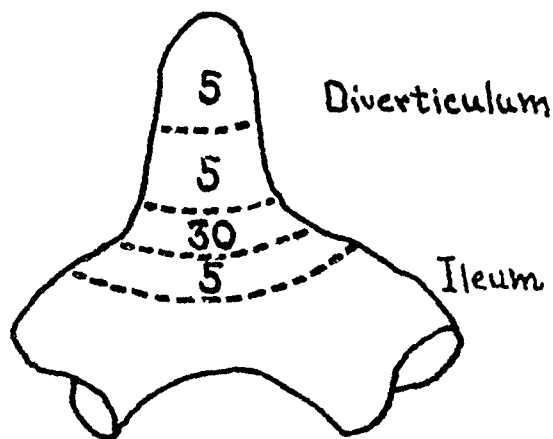


FIGURE 1. Diagram Showing the Various Sites of Ulceration in 45 Cases in Which the Ulcer Sites Were Specified.

(Fig. 1) based on figures by Cobb¹² graphically portrays the relative incidence of the various ulcer sites.

The symptomatology of Meckel's diverticulum is primarily that of the underlying pathologic condition and falls into the following groups: inflammatory; obstructive; ulcerative, with and without perforation; and neoplastic. This study will be limited to a discussion of the ulcerative group.

In the cases of ulceration with perforation, the symptoms are those of peritoneal irritation: namely, abdominal pain, nausea, vomiting, tenderness and muscular rigidity. The resulting inflammatory processes are likely to be well localized.⁹

In ulceration without perforation, the cardinal symptom is hemorrhage. The bleeding may be

*Member of courtesy staff, Hale Hospital, Haverhill.

slight, periodic or intermittent over a long period of time, or it may be sudden and profuse, accompanied by the symptoms of severe blood loss. The character of the expelled blood is frequently of great diagnostic significance,¹³ for it is unlikely to be so dark or tarry as that from bleeding in the upper gastrointestinal tract or so bright red as that from hemorrhage of the colon.

Pain is a variable symptom but, if present, is usually located at the umbilicus. It may be periodic and related to meals but, unlike the pain of gastric or duodenal ulcer, is not relieved by food. Pain may be noted for the first time with or after hemorrhage and is then usually cramplike.

Tenderness and muscular rigidity are usually absent, but palpation frequently produces some feeling of abdominal discomfort.

The following case report of a Meckel's diverticulum with ulceration demonstrates the importance of the cardinal symptom of hemorrhage in unperforated cases. It is noted here in all its variations in a young man over a three-year period, with absence of any other symptoms.

CASE REPORT

A C, a 24-year-old telephone lineman, was seen for the first time in November, 1937, by one of us (A S). His chief symptom was bloody stools, which he had noted for several days, following what he believed was a "grippe" infection. There was no history of a gastrointestinal upset or of any symptoms that usually accompany disease of the gastrointestinal tract.

Physical examination was negative except for a soft systolic murmur heard at the apex of the heart and not transmitted, and a moderate anemia. The red-cell count was 3,400,000, with a hemoglobin of 65 per cent, and the white cell count 9000, with 65 per cent polymorphonuclears and 35 per cent lymphocytes. The blood smear was consistent with a microcytic anemia.

The rectum was cleansed by a saline irrigation, this was followed by a proctoscopic and sigmoidoscopic examination, which revealed no abnormality of the rectum or sigmoid other than a slight trickle of blood and the presence of small clots beyond the tip of the sigmoidoscope. Liquid rest was advised and a modified Sippy regime instituted. The stools gradually cleared of blood. The red cell count, which at first had dropped to 2,300,000 with a hemoglobin of 45 per cent, gradually rose so that at the end of 2 weeks it was 4,000,000, with a hemoglobin of 65 per cent. During this period there were no abnormal findings on repeated physical examination. A complete roentgen ray examination of the gastrointestinal tract showed no evidence of intrinsic disease.

In view of the negative findings, a diagnosis of either Meckel's diverticulum with ulceration and hemorrhage or a solitary bleeding polyp of the colon was entertained. Further roentgen ray study was advised either to confirm or rule out these conditions, but was not accepted.

There were no further bleeding spells until August 16, 1939, when a moderate-sized bloody stool was observed, unaccompanied by any subjective symptoms. Physical examination again yielded negative results. The red-cell count was 4,500,000, with a hemoglobin of 75 per cent, and the white-cell count 7600, with a normal smear. The fol-

lowing morning the stool was normal except for a few streaks of blood coating the fecal mass. The patient consented to a re-examination of the colon by a contrast barium enema. This showed no abnormality. Further roentgen ray examination of the gastrointestinal tract with special study of the small bowel was again advised, but was declined.

In view of the repeated intestinal hemorrhages with a lack of any other symptoms, the repeated absence of physical findings and the negative results obtained from blood studies and roentgen ray examination, an exploratory laprotomy seemed justifiable. This was advised, but the patient refused operation. He continued his bland diet of six meals a day, and in addition took 50 mg of vitamin C three times a day. Small amounts of blood were noted at times in the stool, but the patient continued at his work.

On the morning of October 2, 1940, the patient noted a small bloody stool, but went to his work as usual. Later, while at work, he suddenly felt weak and dizzy. Although these sensations lasted but a short time, he decided not to continue his work and drove a truck 9 miles to the company's garage. During the journey the weakness and dizziness recurred, accompanied by rectal incontinence. He was able to reach the garage and, without assistance, drove another 7 miles to his home. He was seen shortly afterward by one of us (A S) lying on a divan, his trousers and shoes covered with a dark, foul smelling, bloody discharge. The temperature was 97.6°F, the pulse 84, and the blood pressure 132/90. The patient's color was good, and there was no pain or distress. No further bowel movements occurred until late that night, when the patient again felt weak, perspired freely and had two large, dark, foul smelling, bloody movements. Examination showed a pale, perspiring individual whose pulse was weak, with a rate of 60, the blood pressure 86/60. One fourth gram of morphine sulfate was administered subcutaneously, and the patient was transported to the hospital.

On arrival he appeared somewhat better; his pulse rate was 96 and of good quality, and he complained of thirst. The following morning his condition was unchanged, the pulse was 96 and of good quality, and the blood pressure was 114/70. The red cell count was 3,400,000, with a hemoglobin of 50 per cent, and the white-cell count 19,000, with a normal differential. There were no recurrences of bloody stools during the next 36 hours.

During the afternoon of the 2nd hospital day there was a recurrence of weakness, accompanied by perspiration, slowing of the pulse rate and dropping of the blood pressure, with a free rectal discharge of dark, foul smelling blood. Morphine was immediately administered and a transfusion of 500 cc. of citrated blood was given, followed by a continuous intravenous infusion of 5 per cent glucose in physiologic saline solution. As a result of these measures an improvement was noted. The following morning, although no recurrence of bleeding had taken place, the patient appeared much paler and the red-cell count was 1,200,000, with a hemoglobin of 18 per cent.

One of us (H. G. N.) saw the patient in consultation. Since active bleeding had apparently ceased, it was decided to resort to daily blood transfusions in the hope of getting the red-cell count up to at least 3,000,000 before operation, but to operate immediately in the event of a recurrence of bleeding. This course was pursued. A daily transfusion of 500 cc. of citrated blood was given. There were no recurrences of bleeding and the red cell count

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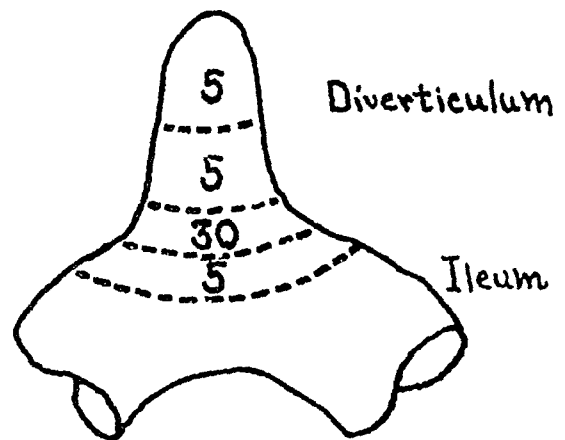


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EXPERIMENTAL STUDIES

Interesting reports have appeared describing the study of *Treponema pallidum* with the electron microscope. Wile, Picard and Kearny⁶ have found that some spirochetes are enclosed in a continuous envelope of unknown nature. Flagella were sometimes seen attached at various points along the sides of the organisms, but not at the ends. Curious knoblike structures were described, which were held to be integral parts of the organism because of their uniform shape and density. Morton and Anderson⁷ have published similar findings. These investigators also found that some of the granules or knoblike structures were apparently in various stages of separation from the spirochetes. In some organisms constrictions were observed that were interpreted as the possible beginnings of transverse division.

Studies on the relation of vitamin C (ascorbic acid) to arsenical sensitivity have been continued by numerous investigators. Delp and Weber⁸ studied plasma vitamin C levels in untreated syphilis, patients under routine antisyphilitic therapy and cases that had shown definite arsenical sensitivity. Vitamin C levels were found to be unaffected by routine therapy. It was impossible to predict sensitivity from plasma vitamin C levels. Improvement in arsenical dermatitis, brought about by treatment with vitamin C, seems to be due to a forced increase in the plasma vitamin C levels. Bundesen and his co-workers,⁹ following the finding that ascorbic acid inhibits the oxidation of the arsphenamine radical, patch-tested known sensitive patients with a mixture of vitamin C and neoarsphenamine. Of 38 patients who showed strongly positive patch-test reactions to neoarsphenamine alone, 32 exhibited negative patch-test reactions with the addition of vitamin C. Vitamin C plasma levels had no effect on the reactions. It was the belief of these workers that patients who showed a positive patch reaction to a mixture of 30 per cent neoarsphenamine and 10 per cent ascorbic acid could probably not be desensitized by means of vitamin C. It is to be hoped that this approach may be utilized to detect which patients can safely continue treatment, with the help of vitamin C, even though they have become sensitized to the arsphenamines. Cormia¹⁰ has reported on the clinical use of ascorbic acid in arsenical sensitivity. He found vitamin C beneficial in the treatment of arsenical dermatitis and useful in the prevention of further reactions.

SEROLOGY

A great deal of work is continuing in the attempt to eliminate so-called "false-positive" serologic errors. Cardon and Atlas¹¹ have called atten-

tion to their discovery that biologic false-positive serologic reactions were observed in 8 (23 per cent) of 34 cases of hyperproteinemia and hyperglobulinemia associated with a variety of conditions, such as chronic pyelonephritis, cirrhosis of the liver with alcoholism, otitis media with erysipelas, pneumonia, acute pyelonephritis, paraplegia and dehydration. This is compared with a normal incidence of 1 false-positive reaction in every 4000 normal persons. Where a false-positive reaction is suspected, it may be well to institute blood-protein studies; increase in either the total serum protein or the serum globulin or both, in the presence of an associated anticomplementary Wassermann reaction, is strongly suggestive of a biologic false-positive reaction.

Kahn¹² has modified his "verification" test for syphilis for the differentiation of specific and non-specific serologic reactions. This author has previously described a verification test based on a differential-temperature technic. The present modification of the test relies on the observation that specific and nonspecific reactions are affected differently by certain concentrations of sodium chloride. It is thought that this removes the limitations of the differential-temperature technic. Kahn states that the present method makes possible the typing of either precipitation or complement-fixation seropositive reactions on the basis of their specificity. Chargin and Rein¹³ report their failure to achieve anything like consistently satisfactory results with the use of Kahn's technic. It is hoped that the performance of the latter's new modification will be more uniformly applicable as a verification procedure.

An interesting study was carried out by Burney, Mays and Iskrant.¹⁴ Eleven apparently nonsyphilitic dementia praecox patients were inoculated with malaria and all subsequently had at least one positive serologic test for syphilis. Eight different serologic technics were employed, some being carried out by more than one laboratory. The Hinton test was the only one that showed no positive reactions; there were, however, three doubtful reactions. No positive or doubtful reactions to any of the tests were returned on the negative controls. The greatest proportion of positive reactions occurred fifteen to twenty-one days after the clinical onset of the malaria. With one exception the positivity did not extend over a period of longer than four weeks. This study again emphasizes the importance of ruling out malaria in regions where this disease is endemic before making a diagnosis of syphilis based on serologic reactions alone.

The present status of biologic false-positive serologic tests for syphilis is most adequately summed up in an editorial¹⁵ that seems a more valuable

statement of facts than any paper reviewed. It did not seem possible to abstract this short dissertation satisfactorily, but one statement seems well worth remembering: "The reactivity of normal human sera with flocculation antigens is usually only minimal in degree, requires refined techniques for its demonstration, and is usually not apparent in the diagnostic tests." For all practical purposes, this refutes the popular conception that many false-positive tests are being reported. When the editor quoted used the term "diagnostic tests" he referred to the standard laboratory procedures such as are relied on by the average practitioner. It is only in institutions where serologic research is carried on that the previously mentioned refinements are obtainable.

A serologic technic for the titration of minute traces of reagin has been described by Lund.¹⁶ This holds great possibilities for the solution of the false-positive problem. It may place the serology of syphilis on a quantitative scale that far exceeds the scope of standard tests.

In former years there was an oft-quoted belief that serologic tests for syphilis are not reliable during pregnancy. Many have long known, however, that this was a false impression. Kandler¹⁷ reports a serologic study of 10,354 pregnant women. Several serologic technics were employed, and it was found that the degree of sensitivity was higher than in nonpregnant women. The specificity of the tests was not impaired, as there were but 0.20 to 0.32 per cent nonspecific reactions. This should silence any further comment on the unreliability of serologic tests for syphilis in pregnancy.

CLINICAL PROBLEMS

Transfusion syphilis. In previous progress reports it has been brought out that citrated whole blood, after a few days' refrigeration, is suitable for transfusion without danger to the recipient, even though syphilitic donors may have been employed. Turner, Bauer and Kluth¹⁸ have now shown that desiccated blood serum is also safe under the same circumstances. Their work was carried out with the spirochetes of both syphilis and yaws, and rabbits were utilized as test animals. All the control animals developed syphilis. After freezing and drying, from six to sixty-five times the amount injected into controls produced no syphilis. Therefore *Treponema pallidum* is commonly killed by the process of freezing and desiccation, even when the method is such that the viability of many bacteria and viruses is retained. It would thus seem that the transfusion of desiccated blood serum or plasma is probably without risk regarding the transmission of syphilis or yaws,

even though the material is obtained from infected donors.

Accidental infection. Leifer¹⁹ reports the cases of two dentists who presented paronychia of the left index-finger nail fold. Both had epitrochlear and axillary adenopathy. The first case went unrecognized until secondary syphilis developed two months later. Profiting by this experience, the author then utilized his heightened index of suspicion and diagnosed the second case by dark-field examination when the chancre was only two weeks old.

Infectious relapse. Eighty cases of infectious relapse were reviewed by Kern.²⁰ About two thirds of these relapses occurred in the first year after the end of treatment, and 80 per cent within the first two years. Relapses were most frequent in patients whose treatment was begun in the primary stage. Suboptimal therapy was followed by the greatest number of early relapses, their frequency decreasing as the total of arsenical injections increased, as one might expect. Kern believes that irregularity of therapy is unimportant as compared with inadequate amounts of treatment. He observed, however, that irregularity accounted for 75 per cent of relapses occurring after the first twenty injections of arsenic. These findings emphasize what we have again and again stressed in these progress reports: namely, that continuous treatment in adequate dosage is essential for the cure of early syphilis.

Osseous syphilis. It is probably a common tendency to think of destructive bone changes as manifestations of late syphilis. Statistically this is justified, but a report by Reynolds and Wassermann²¹ emphasizes the occurrence of destructive osseous lesions in early syphilis. Fifteen cases of osteitis, osteoperiostitis and osteomyelitis have been reported from the Johns Hopkins Hospital. This is an incidence of 0.15 per cent in 10,000 cases of early syphilis. The writers gathered 15 more cases from the literature. The bones of the skull were involved most frequently; those of the sternoclavicular region were next in frequency. Pain and localized tumefaction were the commonest symptoms, but varied according to the degree of periostitis. Pain was worst at night, but some cases were completely asymptomatic. Lesions of the bone occasionally preceded, rather than followed, the secondary eruption. Early syphilitic lesions, even when destructive, responded to treatment with prompt healing, leaving no residual evidence of their existence. It is interesting to call to mind the peculiar stubbornness often encountered in osseous lesions late in the disease. The osteomyelitis of late syphilis is also likely to be a source of diagnostic confusion, simulating such other condi-

tions as sinusitis, metastatic carcinoma, Paget's disease, osteitis fibrosa cystica, as brought out by Alexander and Schoch.²² These authors advocate a therapeutic trial in all problematic bone lesions with positive serologic tests for syphilis, before radical therapy is instituted. This is excellent advice.

Cardiovascular syphilis. The early diagnosis of syphilitic aortitis has been the subject of many dissertations. Kampmeier, Glass and Fleming²³ believe that the clinical diagnosis of uncomplicated syphilitic aortitis is, for all practical purposes, impossible. A report by Boharas, Hollander and Goldsmith²⁴ supports the contention that a positive clinical diagnosis of early syphilitic aortitis is nearly impossible. After a comparison of three technics of radiologic measurement it was concluded that a reliable diagnosis could not be made before a wide dilatation of the aorta had occurred. These authors go so far as to assert that a positive diagnosis of cardiovascular syphilis can be made only in the presence of saccular aneurysms, of aortic regurgitation appearing for the first time in middle-aged syphilitic patients, or of a diffusely dilated aorta without aortic regurgitation or hypertension, past or present. The asymptomatic phase of syphilitic aortic insufficiency was studied by McDermott, Tompsett and Webster.²⁵ Aortic insufficiency without aneurysm was found in 91 (4.5 per cent) of 2018 patients. Half these patients denied any symptoms of cardiac insufficiency at the time of diagnosis. It was possible to follow 28 patients for more than two years; 2 died of heart disease and only 2 others developed symptoms. The aortic width as judged from roentgenograms and fluoroscopy was normal in 43 per cent of these patients. The authors believe that this condition is frequently present in clinically recognizable form for long periods of time before the development of symptoms, and that the prognosis concerning the average duration of life is better than is usually believed. Bruenn²⁶ has published a dissertation on syphilitic occlusion of the coronary arteries. He believes that this diagnosis when made in the absence of signs of aortic insufficiency is likely to be wrong. Pain is a symptom of coronary insufficiency, but can occur with syphilitic aortic insufficiency without the presence of narrowed coronary ostia. Electrocardiograms and x-ray studies are said to be of no aid in differentiating syphilitic aortic insufficiency, with or without syphilitic closure of the coronary ostia. Treatment is of little avail and arsenicals are to be avoided. The prognosis is poor; patients rarely survive three months after the onset of pain; and death usually occurs suddenly. The author also discusses syphilitic lesions of the heart muscle.

Ocular syphilis. The unwarranted fear of arsenical therapy felt by many ophthalmologists was dissipated at a conference of therapy at the Cornell University Medical College and New York Hospital,²⁷ where it was stated that adequate proof exists that arsenic has no deleterious effects on the eye. Lesions of syphilis in the eye, so far as fundamental pathologic changes are concerned, are the same as syphilitic lesions elsewhere and should respond to the same chemotherapeutic measures. Iritis, uveitis, iridorecurrences, optic atrophy, choroiditis, optic neuritis and interstitial keratitis were discussed. In large groups of patients with iritis treated with arsenic, none became blind, whereas in several comparable series of cases given inadequate arsenical therapy blindness resulted in 9 per cent of the patients. Iridorecurrences are of special importance, as it has been found that 20 per cent of these are accompanied by neurorecurrences. In a series of 250 cases of untreated optic atrophy 90 per cent of the patients became blind in three years. Statistics were quoted as indicating that with malarial therapy as few as 12 per cent need become blind. It was brought out that some cases of interstitial keratitis may have permanent incapacitating scars even after intensive routine treatment plus fever therapy, but that such scars can be approached by means of corneal grafting. The need of co-operation between ophthalmologists and syphilologists was prominently stressed. This is timely. A large part of the data on optic atrophy quoted by the Cornell group was taken from the work of Moore, Hahn, Woods and Sloan,²⁸ who have published an exhaustive study of 250 cases. These men thought it probable that the fundamental process in optic atrophy is the same in all types of neurosyphilis and becomes bilateral soon after the onset of symptoms. Their data suggested that it can be prevented by adequate routine therapy of early syphilis. This type of therapy with trivalent arsenic and bismuth is useless after the onset of optic atrophy. Fever therapy (malaria in this series) was held to be the only efficacious method of approach. If visual failure progresses in spite of fever, no other treatment is likely to be effective. Swift-Ellis therapy was found to be of only dubious value in an occasional patient, and probably should be abandoned. So much variation was found in the course of optic atrophy that could not be accounted for by differences in treatment alone that some other additional factor was believed to be of importance in determining the outcome. In studying the types of field defects, it was thought that prognosis is less favorable in the presence of central or paracentral scotomas. Assinder²⁹ has reviewed 6839 ophthalmologic cases, in which syphilis was suspected,

that came under his observation in a period of fifteen years. One thousand and fifteen patients were found to have varying degrees of positivity of the Wassermann reaction. This large group was broken down, and the various types of lesions are discussed.

Neurosyphilis. In the last several years a series of papers has been published as a result of a "co-operative clinical study" of syphilis in five major clinics. The last publication in this series is a study of symptomatic neurosyphilis by Kierland, O'Leary and Vandoren.¹⁰ An evaluation of the therapy of 2019 cases is presented, covering the six major types of neurosyphilis. Each case was observed for not less than two years. The three early types of neurosyphilis are meningal, meningo-vascular and vascular. The three later types are tabes, paresis and taboparesis. The types of therapy used are routine, intraspinal, Tryparsamide, malarial and artificial fever. It was found that negative serologic tests for syphilis in the presence of positive cerebrospinal fluids occurred most frequently in tabes (24 per cent) and least frequently in meningal syphilis (11 per cent). The greatest number of so-called "fixed" positive cerebrospinal fluids were found in paresis and taboparesis. Malarial therapy was found to be the most effective in obtaining clinical improvement and in preventing progression of the disease. Intraspinal therapy, however, appeared to be the most effective means of reversing positive cerebrospinal fluids. From this it is easy to deduce that some cases may require the employment of both these complementary methods of therapy. The studies of this co-operative clinical group have indeed been productive of much valuable and illuminating material.

Tabetic cord bladder. Continuing work previously quoted in these progress reports, Emmett and Beare³¹ have by this time studied 419 cases of tabes with symptoms referable to the urinary bladder (42.4 per cent of 987 tabetic patients). One hundred and eleven male patients were subjected to cystoscopic examination, and 61 of these (55 per cent) had definite obstruction of the vesical neck. Thirty-five were subjected to transurethral prostatic resection. In the majority of cases it was difficult to decide whether vesical dysfunction had been the result of primary neurogenic atony, obstruction of the vesical neck with secondary atony or a combination of the two. The results of transurethral resection were gratifying and incontinence was never produced by the operation itself. The data obtained from this study led the authors to conclude that fibrosis or contracture of the internal (vesical) sphincter, or obstruction in this area, produced by enlargement of the prostate gland, is most likely to be responsible for urinary retention and difficult micturition. In concluding

they state, "Any tabetic patient who has difficulty in voiding, incontinence (especially of the overflow variety), residual urine and some demonstrable obstruction of the vesical neck has an excellent chance of relief of symptoms by complete transurethral resection." The same problem was studied by Nesbit and Gordon,³² who also believe that the modern treatment of the autonomous neurogenic bladder should be directed at surgical relief of the outlet obstruction. Emphasis is laid on the fact that the internal sphincter shares in the hypertonicity of the bladder, through destruction of neurogenic control, and acts as an outlet obstruction. An early approach is advocated by means of transurethral sphincterotomy, which has yielded gratifying results in the hands of these investigators, particularly when undertaken before the bladder has decompensated. Obviously if prostatic obstruction is also present, it could be relieved at the same time. This urologic approach to a serious problem in the management of the cord bladder is one that has been most worth while, and these two groups of workers should be complimented.

Congenital syphilis. Interesting statistics have been published by Wile and Mundt³³ on 500 cases of congenital syphilis. Ninety-eight of these patients were under two years of age; the most striking feature in this group was the finding of positive spinal fluids in 9 (47 per cent) of 19 cases in which punctures were done. Thirty-eight per cent of these infants exhibited developmental bone stigmas. Thirty-three per cent had some adenopathy. Five deaths were attributed to syphilis. Four hundred and two cases were tardive (over two years old). Fifty-nine per cent of these patients had eye lesions, and 37 per cent of these exhibited defective vision. Thirty-one per cent showed Hutchinsonian teeth. Thirty-nine per cent had bone lesions (4 per cent were active). In 343 tardive cases in which spinal fluids were obtained, 27 per cent were positive; half these patients were completely free of signs or symptoms of neurosyphilis. It is to be hoped that these findings will serve to place more emphasis on the need for thorough study of every case of congenital syphilis. Since there should be a decrease in the incidence of congenital syphilis as control of this disease progresses, and since fewer frank congenital lesions are now observed than formerly, it becomes even more important to watch carefully for physical evidence of the disease.

Brauer and Blackstone³⁴ have reported on the dental aspects of congenital syphilis. They undertook their study to determine the relative incidence of dental stigmas in both deciduous and permanent dentition. In contrast to the generally held view that syphilis does not cause changes in

deciduous dentition, these authors found changes that they believed could be due to syphilis in the deciduous incisors of 6 (37 per cent) of sixteen cases. Some enamel hypoplasia was also found in the posterior teeth. Twenty-four (63 per cent) of 38 patients showed syphilitic changes in the permanent incisors and 14 (37 per cent) in the molars. These children had been treated by the usual methods. In a dental study published by Johnston, Anderson and McAlenney,³⁵ the most constant characteristic malformation found in a series of 39 cases was dwarfing of the entire tooth and lack of development of the premaxillary bone, with incisors, canines and first molars usually showing such changes. These authors were unable to demonstrate spirochetes in any of the dental tissues. They state that it is still undetermined whether the spirochete acts directly and specifically in the production of dental anomalies commonly associated with congenital syphilis.

Some very pertinent points are brought out in a survey by the Ingrahams and their co-workers.³⁶ This group approached the problem of congenital syphilis from the preventive standpoint in an attempt to improve the attendance of pregnant syphilitic women in their clinic. The point was made that by means of an ante-partum syphilitic clinic, conducted as part of an obstetric service, more regular attendance would be achieved than if pregnant syphilitic women merely comprised part of the patients received by a large general syphilis clinic. It was further held that when postnatal medical supervision of the infant is carried out in a special session of the pediatric clinic or as part of the routine in a large general syphilis clinic, the results are not so good as those where a "family syphilis clinic" is maintained. Such a family clinic, as carried out by the authors, cut the elapsed time between the first visit of the pregnant woman and the beginning of treatment by two to four weeks. It also created a 100 per cent increase in the number of syphilitic pregnant women receiving regular therapy. It was thought that the proper medical follow-up could be accomplished only by a pediatric division in the family syphilis clinic or through the attendance of a syphilologist in the pediatric clinic. Stress was laid on the importance of having the same experienced follow-up workers care for the mother during pregnancy and follow both mother and child after delivery on the two services (obstetrics and pediatrics), a special family clinic being still better. This is a most worth-while report, and it should be read in full by all clinic executives, social workers, and obstetricians and pediatricians who are connected with syphilis clinics.

THERAPY

No current review of syphilis would be complete without mention of the second edition of Moore's³⁷ book on treatment. All phases of therapy of the many types of syphilis and its complications are clearly, comprehensively and authoritatively covered. The work on massive therapy is objectively reviewed. The author is apparently not an advocate of the five-day drip method of intensive treatment. He states that this has no advantage over conventional methods from a public-health standpoint since infectious relapses have occurred in 12 per cent of the cases. It is pointed out that, in spite of the admitted shortening of the treatment, the results have been attained at the cost of an enormous increase in danger to the patient, as shown by a fourfold increase in fatalities and a two hundred and twenty-fivefold increase in the incidence of hemorrhagic encephalitis. In addition to two new chapters and complete revision of several others, many items are added, such as sections on infectious syphilis in relation to treatment, the oral use of bismuth, mechanical fever therapy, erythema of the ninth day and congenital neurovascular and cardiovascular syphilis. This book should be readily available in the libraries of all who treat syphilis.

A new compound, bismuth ethyl camphorate, which was brought out by Thurmon³⁸ a few years ago, has been further studied by the same author³⁹ from the standpoint of excretion. He found this drug to be an extremely valuable adjunct to the arsphenamines in the treatment of syphilis. When administered in 2-cc. doses at seven-day intervals, bismuth ethyl camphorate maintains the desired level of bismuth in the circulation for a sufficient period to fall within the accepted standards of therapeutic effectiveness. Alexander and Schoch⁴⁰ have published a paper on the use of this same drug in 26 patients with early syphilis in which they began treatment with it. Fourteen cases were primary and 12 were secondary. *Treponema pallidum* promptly disappeared from the surface of lesions after institution of treatment, and healing began after the second day. The low toxicity of the preparation was confirmed. There were a large number of serologic reverses, which speaks well for the therapeutic effectiveness of this drug.

With the advent and rapidly spreading use of the sulfonamide drugs, a fear arose in many minds that the concurrent administration of these compounds with various antisymphilitic remedies might lead to serious toxic complications. A number of papers have appeared that serve to dissolve this apprehension, but only one will be mentioned. Brunet, Shaw and Reinhardt⁴¹ have reported on

the treatment of 44 patients with both syphilis and gonorrhea. These patients each received an average of 63 gm. of sulfanilamide, 6 gm. of an intravenous arsenical (four different drugs) and 2.5 gm. of intramuscular bismuth. No increased incidence of reactions from any of the drugs employed was observed.

The massive arsenical therapy studies that have been conducted in recent years have increased apace. Mounting incidence of syphilis under war conditions has provided more and more material for this investigation. In the 1941 progress report mention was first made of the multiple-syringe technic as a modification of the five-day intravenous drip method. From the same source, Schoch and Alexander⁴² have made a further report. They treated 350 patients by this technic. Two hundred and eight patients were given 120 mg. of Mapharsen daily for ten days, and 142 were given smaller doses over a longer period. Of the 208 treated by the ten-day schedule, 103 were observed for a period of six to eighteen months, resulting in 77 per cent satisfactory results; 11 per cent are pending and 12 per cent were failures. The latter included 3 infectious relapses, 6 serologic relapses, 2 cases with positive cerebrospinal fluids and 1 case of periostitis. Three patients with hemorrhagic encephalitis were encountered, 1 of whom died. The authors considered this technic to compare favorably with the five-day drip method.

Numerous other reports on massive therapy have appeared from various sources, with results roughly paralleling those quoted in the 1941 progress report. A list of references for those interested in this field is appended.⁴³ In an attempt to correlate this work more carefully and develop a short but safe schedule of intensive therapy, and for purposes of orientation, a clinical study has been organized in twelve co-operating clinics, as reported by Eagle and Hogan.⁴⁴ These workers have been studying the problem for several years, both clinically and experimentally. Over 2000 rabbits were given intensive Mapharsen therapy on various schedules. Within broad limits the curative dose was largely independent of the period over which it was administered. Mapharsen by intravenous drip was consistently less effective than when administered by repeated injections over the same length of time. The total amount of arsenic injected without killing the animal increased directly with the time elapsed. It is therefore obvious that the margin of safety (therapeutic index) can be increased by prolonging the duration of treatment. In the twelve co-operating clinics that are now carrying out the clinical study mentioned, three schedules are being tried. All three employ the multiple-syringe technic and vary from four to

eight weeks in duration, with injections of intravenous arsenicals triweekly. Some of the patients are being given concomitant weekly injections of bismuth. The results to date are encouraging with respect to toxicity.

What seems undoubtedly the most authoritative and comprehensive summary of the massive therapy problem is an editorial by Moore,⁴⁵ which was probably written even later than the new chapter in the second edition of his book. The dangers of the five-day treatment are fully stressed, and this program is compared with the treatment schedule suggested by Eagle and Hogan in the preceding reference.

It must be understood that a period of one to three years or longer of carefully controlled study will be necessary before it can be shown that the multiple-syringe technic carries less immediate danger than the five day drip method, or that it would be equally effective on a short term basis. It should be strongly emphasized that massive therapy of early syphilis is still in the experimental stage and unsuitable for general adoption. This point has been stressed each year in these progress reports. The final evaluation of the above methods of therapy must wait many years in order to determine the incidence of late complications, especially cardiovascular syphilis and neurosyphilis. Intensive arsenical therapy by any schedule is so far applicable only to selected cases of early syphilis, and is wholly unsuitable for any stage of late syphilis.

What may eventually prove to be a more outstanding advance in therapy is the combined fever and chemotherapy studies being carried out by Simpson, Rose and Kendell.⁴⁶ For some years these workers have been engaged in the study of artificial-fever therapy, and their present reports are more encouraging than earlier publications. Patients have been evaluated not only from the clinical standpoint, but by follow-up with quantitative serologic studies. Treatment with artificial fever alone was found to be of little value in arresting the progress of early syphilis. The subsequent institution of chemotherapy, alone or combined with fever therapy, was followed by a prompt fall in the quantitative titer and by clinical improvement. Combined fever and chemotherapy given biweekly did not seem to be more effective than weekly administration. The course of fever therapy consisted of ten to twelve treatments combined with the injection of an arsenical preparation and a bismuth compound. Following the course of combined fever and chemotherapy, injections of arsenic and bismuth were continued concurrently for twenty additional weeks. Clinical or serologic relapse has not occurred in this group of patients

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29011

PRESENTATION OF CASE

A fifty-six year-old author came to the hospital because of crampy abdominal pain, nausea and vomiting.

Beginning six months prior to admission he was often awakened because of crampy abdominal pain that was usually followed by nausea and at times by vomiting. During the day he usually felt better, but was bothered by "bloating," eructations and belching. An x-ray study one month later demonstrated "colitis." One month before entry he developed constipation and often passed large amounts of gas by rectum. These symptoms were particularly noticeable since, following the resection of a fistula in ano fifteen years previously, he had never been completely continent of feces and movements tended to be loose. Five days before admission he became very constipated and suffered with extreme abdominal cramps, and subsequently his abdomen became distended. His physician treated him with repeated enemas, and some relief followed expulsion of gas. Three days later he began to vomit a thin fluid, which did not contain blood or coffee grounds and did not have a fecal odor. He had never noted tarry, bloody or acholic stools and had never been jaundiced. During the three months prior to admission he lost 20 pounds. For many weeks he was accustomed to drink as much as a pint of rye whisky each day "to relieve nervousness and insomnia," but this was discontinued during the week prior to admission.

The family and past histories were noncontributory.

Physical examination revealed a very ill, dehydrated man who grunted with each breath. The mucous membranes were pale, dry and cracked. Examination of the heart and lungs was normal. Both diaphragms were elevated to the fourth rib anteriorly, and chest movements were limited. The abdomen was enormously distended and tympanic throughout; no tenderness or spasm was demonstrated, and no masses were felt. The peristaltic sounds were weak and almost absent. No masses were felt on rectal examination, and sphincter control was absent.

The blood pressure was 122 systolic, 80 diastolic. The temperature was 99.1°F., the pulse 94, and the respirations 21.

Examination of the blood revealed a hemoglobin of 10.5 gm., red-cell count of 3,060,000 and a white-cell count of 16,700. The urine was cloudy, amber and acid in reaction, had a specific gravity of 1.010 and gave a ++ test for albumin, a green sugar test and negative tests for diacetic acid, acetone and bile; the sediment contained only amorphous urates. On another examination it gave a + test for albumin and contained a rare red cell, 10 white cells and 4 epithelial cells per high-power field; the sugar test was negative. The blood Hinton test was negative. The serum nonprotein nitrogen was 122 mg. per 100 cc., the chloride 94.6 milliequiv. per liter, and the protein 4.9 gm. per 100 cc. The stool was guaiac negative.

A flat plate of the abdomen demonstrated considerable gas in the dilated stomach and in numerous loops of small bowel, and probably a small amount of gas in the nondilated ascending and transverse colon. There was a large area of calcification overlying the fifth lumbar vertebra.

Many unsuccessful attempts were made to pass a Miller-Abbott tube into the small bowel. Accordingly, after glucose and saline infusions and plasma transfusions, under novocain infiltration, the abdomen was entered through a small oblique incision just to the left of the rectus muscle in the left lower quadrant. The abdomen was explored with two fingers, and a hard mass was found approximately in the midline near the promontory of the sacrum. It was stony hard and was thought to represent the calcified mass of lymph nodes seen in the x-ray. A small tag of omentum presented into the wound and on this were numerous small gray areas suggesting fat necrosis. There was considerable straw-colored free fluid in the peritoneal cavity. A loop of small bowel was drawn into the wound, and a Witzel-type enterostomy was established. The biopsy of omentum showed fat necrosis.

Three days later, the patient seemed slightly improved. The distention was definitely reduced, and the respirations were slower and easier. Peristaltic sounds were more normal on the third hospital day. He was started on a course of intravenous sodium sulfadiazine, totaling 25 gm. in five days. On the sixth hospital day the liver edge was felt three fingerbreadths below the costal margin and seemed rough and uneven. At this time there was definite dullness and consolidation above the high diaphragm on the right side, with increased transmission of breath and voice sounds and occasional rales. The temperature was 99.8°F., the pulse 98, and the respirations 25. The decompression tube was draining a yellowish-brown fluid.

drained from the enterostomy opening. He died on the fortieth day after admission, which is exactly the right time for a patient to die with necrotizing pancreatitis. The patient that almost but does not quite survive pancreatitis is very apt to live just about six weeks.

This man's story is very confusing and it brings up a lot of interesting points. One may hazard a good many guesses about where the underlying pathologic process really was but the chance of being right, so far as I am concerned, is very remote. The patient could perfectly well have had an ileus without having either an intrinsic or extrinsic lesion in the bowel: that is, the ileus could have been on the basis of gastritis and alcoholism. However, he had lost 20 pounds in weight. This man was developing a disease that manifested itself as an acute picture when he came in but actually was an end result of something that had been going on for a period of nearly half a year, possibly longer. It is conceivable that he could have had a reactivation of his mesenteric adenitis. When I saw the first film and read the story, it occurred to me that possibly this was going to turn out to be a gallstone ileus, but I now believe that the film does not have the appearance of a gallstone in a loop of small bowel. One might consider that this was really just cirrhosis of the liver, and pin everything on that as a diagnosis, but there is very little evidence of that. The palpation of the liver, the size of the liver, the ileus and so forth, are compatible but I think such a diagnosis is rather farfetched. The patient could have had, I suppose, some chronic situation in the pancreas that might have led up to an acute episode of this sort, but it seems rather unlikely. It is certainly not the usual history for a man to have a warning six months prior to the time he comes down with pancreatitis, which usually comes out of a clear sky without any long prodromal history. One has to think of tuberculosis, as I mentioned earlier in the discussion, because there is some evidence of certain types of tuberculosis in his past history. I am not sure about the chest; I should suppose that Dr. Holmes would say it was clear so far as any chest lesion is concerned.

That brings us down to the possibility of a lesion in the small intestine of a carcinomatous nature, which might conceivably have been overlooked. It is possible that such a lesion in the small bowel might have been between the point of ileostomy and the portion of the ileum filled from the barium enema. I think that is the most likely diagnosis. The reason I think so is that it is the one area that could not be definitely ruled out by the surgeon and that could not be studied by the x-ray man, using contrast mediums. The next best possibility is some extrinsic neoplasm secondarily involving the

bowel. In this instance I assume that the liver was full of tumor and that is what was the matter with the liver, not cirrhosis.

DR. HOLMES: May I add a few points? In these films it does not look as if the liver conforms to the clinic interpretation. It is a little large but not abnormal in shape. The hepatic flexure is not displaced downward. I wonder if you put enough weight on the fluid in the left pleural space. There was some fluid there earlier, and later a considerable amount.

DR. ALLEN: The patient could have had carcinoma involving the diaphragm, or a primary lesion of the lung, if you choose. I am not worried about the chest picture. In carcinomatosis of the abdomen one often sees fluid in the chest, many times because the diaphragm is studded with carcinoma.

DR. FRANSEEN: The site of the ileostomy was chosen because at the time of the flat film the point of obstruction appeared to be in the ileocecal region and we wanted to reserve the right lower quadrant for the second operation.

DR. DWIGHT L. SISCOE: I followed this patient very closely outside the hospital. Dr. Allen included all diagnoses that we were interested in and considered some more too. There were a few points that Dr. Allen questioned. One was the alcohol. The alcohol made a much greater impression on our minds than the record here would suggest. The roentgenologist who first examined him was greatly impressed by the gastritis and the amount of alcohol consumed. In fact we received word that he had been using a quart a day instead of a pint. So the possibility of cirrhosis was very much in our minds. During the last few days of his life the patient ran a steady downhill course, and a few days before death one observer believed that he felt a mass in the right lower quadrant.

DR. FRANSEEN: The patient was scheduled for operation, but that morning had a large hemorrhage and the operation was called off. That was twenty-four hours before death.

CLINICAL DIAGNOSIS

Carcinoma of stomach?
Portal cirrhosis?

DR. ALLEN'S DIAGNOSIS

Carcinomatosis, involving the lower ileum.

ANATOMICAL DIAGNOSIS

Pancreatitis, hemorrhagic, subacute.
Fat necrosis, extensive.
Rupture of splenic artery and vein.
Erosion into duodenum, with massive gastrointestinal hemorrhage.

Chronic cholecystitis
 Cholelithiasis, with stone in ampulla of Vater.
 Tuberculous mesenteric adenitis, healed.
 Arteriosclerosis, moderate: aortic, coronary and renal

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: At autopsy innumerable foci of fat necrosis covered the peritoneal surfaces from the bottom of the pelvis to the inferior surface of the diaphragm. The entire pancreas had been destroyed, and the retroperitoneal tissues of the upper portion of the abdominal cavity were occupied by a huge blood-filled cavity with shaggy, necrotic walls. Into this cavity dangled the ends of the splenic vein and artery, neither of which was thrombosed. A spontaneous rupture had occurred into the posterior wall of the third portion of the duodenum, so the terminal event was evidently hemorrhage from the splenic vessels into the cavity and hence into the duodenum, filling the gastrointestinal tract with blood. It was interesting that both pleural cavities contained small amounts of clear straw colored fluid so the supposed chest tap must have penetrated into the retroperitoneal cavity. The extremely high diaphragm made this readily possible. The liver was at the upper limit of normal in size, weighing 1800 gm., and was not nodular or cirrhotic. It did show extensive acute central necrosis, which accounts for the terminal liver insufficiency.

This man had the classic setup for acute pancreatitis. There was a severe chronic cholecystitis with innumerable small stones. The prodromal symptoms that led Dr. Allen to trace the onset of his illness back at least six months may well, in retrospect, have been due to his gall bladder. There was likewise a small stone in the common duct partially imbedded in the mouth of the duct of Wirsung. There was thus a real possibility of reflux of bile into the pancreatic duct. It must be admitted, of course, that few cases of pancreatitis show a calculus in the appropriate location.

DR. ALLEN: The straw colored fluid, five days after the pancreatitis started, is the thing that bothered me. Do you believe that that is usual? We frequently do a paracentesis to make a differential diagnosis between pancreatitis and perforated ulcer, and things of that sort, and we rely on the character of the fluid to guide us.

DR. MALLORY: I should consider clear yellow fluid unusual too.

DR. ALLEN: The serum amylase determination, so far as I could tell from the record, was not done till the fifth or sixth day, so that it had to be thrown out as a guide. If that had been done

the first day I think it would have had more significance.

DR. JOSEPH C. AUB: Why does a patient with pancreatitis die on the fortieth day?

DR. ALLEN: It takes just about that long for the pancreas to become completely necrotic and erode a big vessel, usually the splenic artery.

DR. SISCOE: I am sorry Dr. McKittrick is not here to discuss this case, since he held out for the diagnosis of pancreatitis almost from the start. He believed that the intra-abdominal fat necrosis could be explained in no other way.

CASE 29012

PRESENTATION OF CASE

A fifty-year-old man entered the hospital complaining of marked ankle edema of three weeks' duration.

The patient was seen for the first time in the Out Patient Department six months before admission. He stated that about a year and a half previously he had caught cold and that a cough coincident with the illness had persisted and was accompanied by a run down feeling, generalized weakness and increasing exertional dyspnea. About five months later he noticed palpitation and swelling of the ankles, which gradually rose to the knees and scrotum; these persisted, and at the time of being seen he was compelled to sleep using two pillows and to urinate three or four times during the night; at no time had there been any pain, but there was some loss of weight. On examination the patient was emaciated and rather ill-looking, with increased respirations, slight cyanosis of the lips, venous distention in the neck and over the abdomen and edema of the lower legs and scrotum. The chest was deformed (no description noted), and although the heart was not enlarged to percussion, its rate was 100 with an occasional extrasystole and a diffuse apex beat. The examiner believed that he heard a soft systolic murmur and a questionable presystolic murmur at the apex. The blood pressure was 95 systolic, 60 diastolic. There were a few rales at the lung bases, and the liver was percussed four finger-breadths below the costal margin.

The urine was negative, and the blood showed a hemoglobin of 16.9 gm. and a normal smear. One sputum examination was negative for tubercle bacilli. The electrocardiogram showed a normal rhythm with a rate of 85 and a PR interval of 0.13 second. P₂ was prominent, and there was marked right-axis deviation; S₂ was prominent, and ST₂ and ST₃ slightly sagging; T₄ was low, with an absent R₄.

On x-ray examination the diaphragm was low and limited in motion on both sides, and the lung fields were very bright. Rather sharp linear mottled areas of increased density and numerous small and large blebs were visible in the upper lung fields. There was marked depression of the lower end of the sternum; the heart was not particularly abnormal.

The patient was sent home to bed on digitalis and a low-fluid and low-salt intake; mercurial diuretics were administered in the Out Patient Department. He visited the hospital each week, and although a curtailment of activity brought about some improvement, dyspnea, venous congestion, cyanosis, basal rales and peripheral edema were always present in varying severity.

The right border of the heart was percussed 2 cm. to the right of the sternal border, whereas the left border was within normal limits. The rhythm was normal, with an occasional premature beat. The sounds were distant, and it seemed to be the consensus that there was no presystolic murmur and that the systolic apical murmur was not always heard. The blood pressure varied from 115 to 90 systolic and from 90 to 60 diastolic; the pulse averaged 90. Four and a half months before entry an electrocardiographic recording with six chest leads showed a normal rhythm with a rate of 110. The P waves in all leads were inverted; QRS was multiphasic and almost isoelectric; S was of high voltage, being highest in Leads 3 and 4. R_1 was less than 0.5 mm. in all leads. T was inverted in Leads 1 and 2, low to flat in Lead 3 and upright in Leads 4, 5 and 6.

As time passed, cyanosis became a more prominent feature, although it was still possible for the patient to lie flat fairly comfortably. Also, he began to mention nocturnal dyspnea, cough and abdominal distention. Mercurial diuretics continued to increase renal output, but in later months this effect was nullified by prolonged periods of oliguria.

A little more than a month before entry the patient came to the Out Patient Department and was obviously much worse, with an increase in dyspnea, cyanosis, peripheral edema, basal rales, liver size and abdominal distention. Consequently he was sent to a nursing home, but returned later and was admitted to the hospital.

The family history was noncontributory. At twenty years of age the patient had gonorrhea. Twenty-five years before admission he had a sudden sharp precordial pain that occurred while at rest and was severe enough to preclude movement. He was taken to another hospital and told that he suffered from "pleurisy around the heart." Strapping gave great relief and convalescence was uneventful, pain being the only symptom.

On examination the patient was well developed, but emaciated and somewhat confused; he had a hacking cough, which produced frothy, yellow sputum. There was marked cyanosis of the fingers, lips and ears, which seemed out of all proportion to the dyspnea. In the upright position the neck veins were distended and pulsating. The chest showed a marked pigeon-breast deformity and a Harrison groove and because of this it was difficult to percuss the heart, although the right border seemed to be 2 cm. from the sternal margin, and the left border 8 cm. from the midline. The sounds were distant and regular, and a soft systolic murmur was present at the apex. The pulmonary second sound was greater than the aortic. There were percussion dullness, diminished breath sounds and tactile fremitus and moist rales over the lower half of each lung field, but above this, hyperresonance and bronchovesicular breathing. The abdomen was distended and tense, with an everted umbilicus and shifting dullness; the liver edge was three fingerbreadths below the costal margin in the midclavicular line. Pitting edema of the back, sacrum, scrotum and lower legs was present. Examination of the nervous system was negative except for some confusion concerning current events.

The blood pressure was 85 systolic, 65 diastolic. The temperature was 98°F., the pulse 100 and the respirations 30.

The urine was acid in reaction and showed a +++ test for albumin and a + test for bile; the sediment contained 5 to 10 red cells and many white cells per high-power field. Examination of the blood showed an average red-cell count of 5,880,000 with a hemoglobin of 21 gm., and a white-cell count of 7450 with 84 per cent polymorphonuclears. The hematocrit reading was 60 per cent, and the blood bicarbonate 27.2 milliequiv. per liter. The nonprotein nitrogen was 93.5 mg. per 100 cc., and a blood culture was negative.

An electrocardiographic recording showed a normal rhythm with a rate of 100 and a PR interval of 0.16 second. There was low voltage in all leads, with moderate right-axis deviation. T_1 was low, and T_2 and T_3 inverted; there was an elevated takeoff in ST_4 , and an absent R_4 .

The patient was given the usual supportive measures, but death occurred on the third hospital day, with no notable clinical incident in the interim.

DIFFERENTIAL DIAGNOSIS

DR. DONALD S. KING: A clinicopathological conference is like a game of contract bridge. You are dealt a hand. You sort your cards into four suits; history, physical examination, laboratory and x-ray.

You pick out the high cards, which you can depend on to take tricks. Then you try to find out what other players at the table, such as the roentgenologist and the cardiologist, may have to influence your estimate of the situation. And finally you bid everything that you think you can make.

Well let us look at the hand. The history is that of a man of fifty who at twenty-five had precordial pain, which was probably due to pleurisy and is not connected with the terminal illness. Two years before entry he had a cold followed by cough, weakness and exertional dyspnea. These early symptoms were probably pulmonary, not cardiac. Nineteen months previously there was ankle edema, and later, edema involving the scrotum and back, palpitation, orthopnea, nocturia and weight loss. Finally there were nocturnal dyspnea, abdominal distention and frothy, yellow sputum.

The signs were emaciation and a pigeon breast, rapid respirations, cyanosis, — at first slight but becoming marked and out of proportion to the dyspnea, — venous distention in the neck, an enlarged liver and shifting abdominal dullness. The heart examination showed a pulse of 90 to 100 with occasional premature beats. The right border is said to have been 2 cm. from the sternal margin, but in the face of a pigeon breast and emphysema I may be excused for being skeptical. The pulmonic second sound was greater than the aortic, there was a soft systolic murmur, the blood pressure was from 85 to 115 systolic and from 60 to 90 diastolic, and the lungs showed basal rales and, at the last examination, basal dullness with diminished breath sounds and tactile fremitus with hyperresonance above.

The blood showed a moderate degree of polycythemia with a hemoglobin elevated to 21 gm., a red-cell count of 5,800,000 and a hematocrit of 60 per cent. The urine was that of congestion, with albumin, a little bile, a few red cells and many white cells. The nonprotein nitrogen was 93.5 mg., probably a terminal condition, and the bicarbonate level was essentially normal.

The x-ray films showed generalized emphysema, as evidenced by the low flat diaphragm, both sides of which are said to have been limited in motion, and the bright lung fields. Besides there were many emphysematous blebs. There were also what are described as sharp linear mottled areas. I do not like the term "linear mottling" but we can look at the film later and get an idea of what is meant.

In general this is the complete picture of failure of the right side of the heart. With marked cyanosis, distention of the neck veins, enlarged liver, rales, edema and an increased pulmonic second

sound we can bid at least a little slam on that diagnosis.

But we must go farther and try to find the reason why the right heart failed. There are two possible classes of causes — cardiac and pulmonary. The cardiac conditions that may cause congestion of the pulmonary vascular bed and therefore strain on the right side of the heart leading to failure are two: failure of the left side of the heart, as in arteriosclerotic hypertension, and deformity of the mitral valve, usually with stenosis. The possible pulmonary conditions are likewise two: emphysematous changes, which lead to a narrowing of the vascular bed with resultant pulmonary hypertension, and primary changes in the pulmonary arteries themselves. And to continue one step farther, the possible changes in the pulmonary arteries are three: sclerosis, obliterative endarteritis (frequently referred to as Ayerza's disease) and thrombi or emboli.

For the sake of clarity I shall at this point jump to my major clinical conclusion concerning the choice among the six possible causes of right-sided heart failure. I maintain that there is no evidence of left-sided heart failure, of deformity of the mitral valve or of any other condition of the heart itself that would account for the right-sided failure. I am driven then to a diagnosis of chronic cor pulmonale with the primary difficulty in the lungs. Emphysema of marked degree is undoubtedly present, and there have been autopsies in this hospital where such emphysema was the only explanation for pulmonary hypertension and consequent right-sided failure. But we should go farther and try to dispose of the pulmonary vascular conditions that I said might be present.

In the face of emphysema it is unnecessary to postulate pulmonary arteriosclerosis, which it is impossible to prove in any case. Obliterative endarteritis is usually a disease of younger people, and the etiologic factors sometimes found, such as syphilis, rheumatic fever and chronic bronchial infection, are absent. We come then to the last of the possible pulmonary vascular changes — thrombosis or embolism. For some unexplainable reason I want to bring such changes into this picture; there are no symptoms of them, and unless the x-ray films show evidence, it seems to me that we should drop this cause from the list of possibilities.

There is much that we do not know about pulmonary hypertension and its causes. I remember only too well the case of a "black cardiac" given to me in one of these conferences; the patient had all the signs of right-sided failure with much more marked cyanosis than that in the present case, and yet at autopsy Dr. Mallory found almost no struc-

tural changes. If I remember correctly there was moderate sclerosis, but nothing else — no thrombi, not even any demonstrable narrowing of the lumens of the arteries or arterioles. So in the present case I shall, after x-ray conference, probably leave out thrombosis as unnecessary to explain the picture and as incapable of proof.

At this moment, without careful study of the x-ray films and the electrocardiograms, my clinical diagnosis is pulmonary emphysema with emphysematous blebs, probably with fibrosis, and chronic cor pulmonale with right-sided heart failure.

Now to the x-ray films and electrocardiograms to see what other factors they may introduce.

This is the x-ray film, and it is obvious that there are generalized emphysema and emphysematous blebs. The next question concerns the "mottling" in the upper lobes. Dr. Lingley, are the changes in this film consistent with pulmonary fibrosis?

DR. JAMES R. LINGLEY: There is marked emphysema, as described. The distribution of the density is more consistent with tuberculosis than with ordinary fibrosis. It is fibrosis, certainly, but tuberculous fibrosis or fibroid phthisis. A process of this nature involving both apices is tuberculosis in over 99 per cent of cases.

DR. KING: This introduces a new factor, tuberculosis. I am sure Dr. Lingley agrees that we have had cases of idiopathic pulmonary fibrosis that showed lesions involving the upper lobes as well as the rest of the lungs. But I agree with him that lesions predominantly in the upper lobes, like these, are almost always tuberculous.

Do you see evidence of active tuberculosis? It is clear that the outpatient physician had this in mind, because one sputum specimen was examined for tubercle bacilli.

DR. LINGLEY: I cannot express an opinion on that point, as I dislike calling a lesion active without two or more examinations at intervals.

DR. KING: So far then the x-ray has added the fact that tuberculosis is probably the underlying cause of the pulmonary fibrosis that is present.

Now I want to ask one other question. Do you see evidence of pulmonary thrombosis or embolism, or of recent or old infarcts caused therefrom?

DR. LINGLEY: No.

DR. KING: This is as good a time as any to take up another possible factor in pulmonocardiac deaths. The reported cases of chest deformity eventually leading to death are those of extreme kyphoscoliosis. Personally I doubt that the pigeon breast was a significant factor in this case.

What about the x-ray appearance of the heart?

DR. LINGLEY: The heart does not appear enlarged in either the posteroanterior or the lateral

view. However, the very marked depression of the fourth segment and xiphoid of the sternum undoubtedly has produced rotation of the heart. Moderate enlargement could be present and yet not visible because of the degree of rotation. It is surprising that with this amount of depression of the sternum, producing marked pressure on the heart, there is no lateral or posterior displacement.

DR. KING: Because of the low diaphragm and the rotation of the heart, the picture is not inconsistent with right-sided enlargement?

DR. LINGLEY: No; it may be present, but I cannot prove it.

DR. KING: Is the pulmonary artery dilated?

DR. LINGLEY: It is prominent in the posteroanterior view, but again, rotation confuses the picture. The normal pulmonary artery would be prominent in this view if the heart were rotated.

About all the information I can give you is that there are marked emphysema and bilateral tuberculosis, and that the lower sternum and xiphoid produce marked pressure on the heart, rotating but not displacing it.

DR. KING: Finally we have the electrocardiogram. From the clinical standpoint I expect Dr. Bland to say that the electrocardiogram shows right-axis deviation and is therefore consistent with right-sided heart failure. However, Dr. White states that 50 per cent of the cases of chronic cor pulmonale have coronary disease, and I am particularly anxious to know if Dr. Bland believes that the electrocardiogram gives evidence of coronary disease or any findings that cannot be explained on the basis of chronic cor pulmonale.

DR. EDWARD F. BLAND: There is definite right-axis deviation, which is consistent with cor pulmonale. There is no evidence of coronary disease insofar as the electrocardiogram goes.

DR. KING: I am now ready to make the final bid. I shall say: pulmonary emphysema and emphysematous blebs; pulmonary fibrosis, probably on a tuberculous basis, but with no evidence of active pulmonary tuberculosis; chronic cor pulmonale, with dilatation and hypertrophy of the right ventricle; congestion of the liver, with ascites.

DR. S. P. SARRIS: Would you consider pericardial fixation in this case? Could the pain twenty-five years previously have been of pericardial origin?

DR. KING: I do not believe that we can pay much attention to that story of pain, which I interpret as having been due to pleurisy.

I do believe that constrictive pericarditis should be mentioned as a possible cause of the distended veins and liver, with ascites and edema. However,

*White, P. D. *Heart Disease*. 931 pp. New York: The Macmillan Company, 1931. P. 408.

I do not see the evidence for such a diagnosis in this case, and believe that another and more adequate diagnosis has been established.

DR. LINGLEY: In this case, could not the depression of the sternum alone produce *cor pulmonale*?

DR. BLAND: It hardly seems sufficient in this case, but a marked funnel chest can ultimately cause *cor pulmonale*.

CLINICAL DIAGNOSES

Cor pulmonale.
Pulmonary fibrosis.
Cardiac failure.

DR. KING'S DIAGNOSES

Pulmonary emphysema and emphysematous blebs.
Pulmonary fibrosis, probably on a tuberculous basis, but without active pulmonary tuberculosis.
Chronic *cor pulmonale*, with dilatation and hypertrophy of right ventricle.
Chronic congestion of the liver with ascites.

ANATOMICAL DIAGNOSES

Cor pulmonale.
Pulmonary fibrosis.
Pulmonary emphysema.
Thrombosis of left pulmonary artery.
Pulmonary tuberculosis, with cavitation.
Ulcer of cecum, tuberculous.
Pleuritis, fibrous.
Anasarca.
Meckel's diverticulum.
Pigeon breast.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Since Dr. King suggested the analogy with contract bridge I cannot resist, despite the excellence of his discussion, pointing out that in this case he was dealt what is often called a "pianola hand." Most of the possible causes for *cor pulmonale*, phthisis, emphysema, pulmonary fibrosis, pulmonary thrombosis and thoracic deformity were simultaneously present, so he could scarcely go wrong. Which of these various factors played the predominant role is quite impossible to say, and a synergistic action seems most probable.

A note by Dr. Howard Sprague on the patient's first admission runs as follows:

Cyanosis of face and hands. Veins distended, but patient lies flat without much discomfort. Greatly diminished breath sounds, especially over the back; occasional moist rales; heart size impossible to deter-

mine clinically, but not increased according to x-ray films; sounds distant; rhythm normal; a third sound heard; neither aortic nor pulmonic second sound accentuated. Impression: I believe this to be chronic *cor pulmonale* based on pulmonary fibrosis and emphysema, with final congestive failure. I do not find enough evidence for a diagnosis of mitral stenosis. He may have an adherent pericardium, but the pleurisy occurred forty years ago so I do not believe Pick's syndrome is present.

The post-mortem examination showed a high degree of *cor pulmonale*. Both the right auricle and the right ventricle were dilated, and the latter measured 8 mm. in thickness as compared with 13 mm. for the left ventricle. The pulmonary valve ring measured 10.5 cm. compared with 8 cm. for the aortic, and the tricuspid valve was 16 cm. in circumference. The pericardial cavity was entirely free from adhesions, and there was no evidence of mitral stenosis. The lungs showed very advanced bullous emphysema with air sacs ranging up to 9 cm. in diameter in both lower lobes. In addition, both upper lobes and the right middle lobe showed scattered tuberculous cavities lined with caseous material. An additional factor, which must have played a role in the development of the *cor pulmonale*, was the presence of a large old and well-organized thrombus in the left pulmonary artery, which filled approximately two thirds of the vessel. One other evidence of active tuberculosis was an ulcer of the cecum.

Microscopic examination of the lung shows active tuberculosis in the upper lobe. Secretions from the lower lobe show extensive fibrosis and emphysema. There are many military fibrotic lesions that have a tendency to be located in regions usually occupied by lymphatics. A few of these contain giant cells, and all of them have considerable carbon pigment. They could be healed tubercles but are much more characteristic of silicotic nodules. The patient's more remote occupational history was never inquired into so we do not know whether he had exposure to silica dust. Chronic silicosis is, of course, a common cause of *cor pulmonale*. The liver showed an extreme degree of chronic passive congestion, with degeneration of the liver cells in the central two thirds of every lobule but no central fibrosis that would warrant a diagnosis of cardiac cirrhosis. The spleen was very small, weighing 70 gm. An incidental finding was a Meckel's diverticulum 100 cm. from the ileocecal valve; it contained well-differentiated gastric mucosa but no sign of peptic ulceration.

DR. SARRIS: Was any cause found for the pulmonary thrombosis?

DR. MALLORY: No underlying anatomic cause was found.

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UNITED WAR FUND

THE campaign of the Greater Boston United War Fund opened officially on January 4 with a gathering of the members of the Advance Gifts Division at Symphony Hall. The final event, the period of intensive solicitation, will begin on January 21 and end on February 10. During the campaign \$7,800,000 must be contributed to cover the needs of two hundred and thirty-five hospitals and social agencies in forty-nine local communities, and of various wartime services, such as United Service Organizations, United Nations Relief Fund and War Prisoners Aid. The total is slightly greater than set and raised a year ago, a fact necessitated not by the demands of local institu-

tions, which are less, but by those incidental to the war effort.

Although many of the physicians of Greater Boston contribute generous amounts of time and energy to the local charitable organizations, their opportunities to give aid to the wartime services are practically negligible. By subscribing, they will be doing what all clear-thinking and patriotic citizens should do—support the Fund to their utmost.

ERADICATION OF MALARIA

ANOTHER article¹ has been published by the *Reader's Digest* that can only misinform and mislead the public. Unfortunately, the reader is given the erroneous conception that malaria can be eradicated by means of a five-day treatment with the synthetic drug, atabrine. False hopes will be aroused among the inhabitants of the endemic and hyperendemic malarious areas of the world, and wishful thinking among our population and particularly among our troops serving in tropical and subtropical areas will tend to minimize the seriousness of the malaria problem and of the loss of the main source of quinine in the Netherlands East Indies.

Atabrine is the best substitute for quinine that has been developed and utilized for the treatment of malaria. The drug, when properly administered by a physician or by trained personnel under the direction of a physician, cures a higher percentage of cases and lessens the relapse rate to a greater degree than does quinine. The drug can be used prophylactically to prevent clinical malaria but, like quinine, does not prevent infection.

Atabrine produces toxic symptoms in a certain percentage of persons. The drug is also accumulative, being eliminated very slowly from the body. Furthermore, atabrine has no effect on the gametocytes or so-called "crescents" of malignant tertian malaria (caused by *Plasmodium falciparum*) and hence transmission of this infection can take place even while the drug is being administered; in

such cases, a course of plasmochin, the specific for the gametocytes of *P. falciparum*, must be given to sterilize the peripheral blood. And, finally, it is well known among malarialogists that no drug or combination of drugs will produce a cure in all infected patients and thus completely destroy the seedbed of parasites in an urban or rural population where malaria is an acute problem.

The results of two extensive experiments to control malaria are cited to support the above statements. Clark, Komp and Jobbins² attempted to control malaria in a number of endemic areas in Panama over a period of ten years by making monthly parasite surveys and by treating the positive cases with two combinations of drugs—atabrine and plasmochin simplex and quinine and plasmochin simplex. These careful and experienced workers succeeded in greatly reducing the cases of severe clinical malaria but failed to eradicate malaria and to reduce transmission. They also demonstrated that drug-control methods could not prevent an epidemic if great numbers of anopheline mosquitoes were present. Cuica and his collaborators,³ working in Roumania, were also able to reduce clinical cases, relapses and malarial morbidity by the use of atabrine and plasmochin prophylactically and therapeutically. In spite of giving systematic treatment to all cases of malaria, the parasite-carrier rate—the seedbed of the infection—remained about the same. Suspension of treatment after three years was followed by an increase of the clinical cases to the level that had existed before the experiment was started. The latter group also showed that the length of treatment with atabrine should be seven days, and that the drug causes toxic symptoms in a certain percentage of cases, particularly in children under one year of age. They also emphasized that the administration of synthetic malarial drugs should be under medical supervision.

The final solution of the diversity of problems in the control and eradication of malaria does not depend alone on the per capita cost of atabrine or of any other malarial drug. The claims

made for the use of a drug in one area do not necessarily apply to another where the infection may be more widespread and more serious clinically. The cost of mosquito control, where such a program is feasible, is often great, requiring the maintenance of trained field workers (entomologists and engineers) and laboratory and medical staffs. When this item is considered, the cost of malaria control increases greatly and many localities or governments cannot support and maintain the program.

It is quite easy to say, "Thanks to atabrine, the fiendish disabler can now be wiped out, if we will have the will to try." It should be pointed out, however, that the work of malarialogists, entomologists, engineers, chemists and pharmacologists has advanced knowledge greatly during the past decade. Their evidence and advice is informed and reliable and not prone to mislead the public.⁴ These men, many of whom are risking their lives in the study of malaria, know that no ideal drug for the treatment of malaria has been discovered and that no known methods for the eradication of malaria have been successful. And, once again,⁵ it must be emphasized that the editors of periodicals in which articles conveying such impressions are published would do well to consult experts in the fields concerned before releasing them for lay consumption. Articles of this sort do not help, they only hinder, the battle against disease and the winning of the war.

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MEDICAL EPONYM

SNELLEN TEST TYPES

These types were introduced by Dr. Herman Snellen (1834-1908) in a pamphlet published at Utrecht in 1862. Six versions, Latin, English, French, Italian, German and Dutch, appeared simultaneously under the title, *Test Types for the*

Determination of Vision. The following is a translation from the German edition:

In order to determine the visual acuity, we measure the smallest subtending angle at which objects of known size and shape can be distinguished. . . . Square letters, the lines of which are a fifth of the height in thickness, are usually distinctly perceptible to the normal eye when subtending an angle of 5 minutes. The number over the letters expresses in Paris feet the distance at which the letters are seen when subtending an angle of 5 minutes.

The visual acuity (S) [later v] is expressed by the relation of the distance (d) at which the latter is recognized to the distance (D) at which it subtends an angle of 5 minutes.

$$S = \frac{d}{D}$$

If we find d equal to D and consequently No. 20 is seen at a distance of 20 feet, then $S = \frac{20}{20} = 1$; that

is, the visual acuity is normal. If, on the other hand, d is less than D , so that No. 20 is seen only at 10 feet, No. 10 only at 2 feet and No. 6 only at 1 foot, then the visual acuity in these cases is respectively,

$$S = \frac{10}{20} = \frac{1}{2}$$

$$S = \frac{2}{10} = \frac{1}{5}$$

$$S = \frac{1}{6}$$

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL MORTALITY

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

ANESTHESIA

Ten maternal deaths due to anesthesia occurred in Massachusetts during 1941. There were 3 autopsies in this series of cases.

The first case was that of a primipara who after a test of labor was delivered by Waters's cesarean section. While the patient was going under anesthesia, gastric contents were aspirated; blood-tinged sputum appeared one hour after delivery, and x-ray films showed consolidation in the right upper lobe. She was put in an oxygen tent after delivery, bronchoscopy was performed and sulfathiazole treatment was instituted, but death occurred three days after delivery. Autopsy revealed massive pulmonary edema and bronchopneumonia. The patient was given the full advantage of present-day knowledge, and in retrospect the vomiting during oper-

ation can only be looked on as a most unfortunate incident.

The second patient, a multipara who had one living child, entered the hospital in active labor with the head on the perineum. During the administration of nitrous oxide and oxygen anesthesia, which was given by an obstetric supervisor, the patient became black and vomited; the mask was removed, and she regained consciousness; when the anesthesia was again started she became cyanotic and died. Twins were delivered, and both babies lived. It would have been, of course, far better if this patient had been allowed to deliver herself without anesthesia; the vomiting during anesthesia, however, would probably not have occurred if an inhalation anesthetic had not been used. This case raises the interesting question of whether spinal anesthesia should not be more widely used for delivery; in the hands of one experienced in its use it does not carry the danger of nausea and vomiting.

The third case was that of a primipara who had been delivered by low forceps of a living child; during repair of the episiotomy wound, respirations ceased and the patient did not breathe again. According to the medical examiner's report, based on an autopsy limited to the head, this death was due to nitrous oxide asphyxiation. Surely this death was regrettable if not reprehensible.

The fourth case was that of a primipara who, because of cephalopelvic disproportion, was being prepared for cesarean section, which was to be performed under spinal anesthesia. Twenty milligrams of Pontocaine were injected into the spinal canal, immediately following which the respiratory and cardiac centers became paralyzed, and in spite of stimulants, death occurred two hours later. This death was undoubtedly due to spinal anesthesia. This anesthetic was probably not given by an experienced anesthetist, for 20 mg. of Pontocaine is an astoundingly large dose.

The fifth patient, a primipara who was delivered by low forceps, vomited food as she was coming out of anesthesia. Bronchoscopy was performed and pieces of food were removed; but massive collapse of the lung developed, and the patient died four hours post partum. Nitrous oxide, oxygen and ether was used in this case. There is no evidence in the record that any of the barbiturates were used. This fatality emphasizes the danger of inhalation anesthesia when the stomach is filled with food.

The sixth patient, a woman in her third pregnancy and at term, had a separated placenta, which was treated conservatively by rupture of the membranes and packing the cervix. She was delivered by low forceps after full dilatation. She had vom-

ited while going under ether, and bronchoscopy showed evidence of aspiration. In spite of suction, the patient gradually went downhill, and died four hours after delivery. This case merely emphasizes the potential seriousness of vomiting.

The seventh patient was a primipara who was given ether at the very end of labor and for episiotomy repair. During the administration of the anesthetic vomiting occurred; acute edema of the lungs resulted, and death followed in eight hours. Autopsy revealed *bilateral acute pneumonitis with bilateral hydrothorax*. Since this patient was convalescing from an upper respiratory infection when labor started, it is barely possible that the infection had some bearing on the fatality, although it seems more likely that the anesthesia was the determining factor in view of the few hours that elapsed between delivery and death.

The eighth patient, who had two living children, started in labor at home, and the cord prolapsed. She was sent to the hospital in Trendelenburg position. Under nitrous oxide and ether anesthesia version was accomplished and a stillborn child delivered. Cyanosis appeared before delivery of the placenta, and death followed immediately. This must be considered an anesthetic death. Whether or not the long period the patient was in the Trendelenburg position had anything to do with the pulmonary congestion is an academic question.

The ninth patient was a primipara who, while on the operating table under nitrous oxide, oxygen and ether anesthesia, aspirated vomitus into the trachea and lost consciousness, which she did not regain, death occurring ten hours after delivery. Although this patient had had 6 gr. of Nembutal several hours before delivery, it is not quite fair to attribute the fatality in any way to the medication. This case emphasizes the importance of anesthesia administration by trained anesthetists at the time of delivery.

The history of the tenth and final case is inadequate. A patient at term was given spinal anesthesia before cesarean section, and although the death certificate attributes this death to acute cardiac dilatation it was more probably due to the spinal anesthesia.

All these deaths from anesthesia seem to have been preventable as well as unfortunate.

DEATHS

BRACKETT — ELLIOTT G. BRACKETT, M.D., of Boston, died December 28. He was in his eighty-third year.

Born in Newton, he attended Newton High School and received his degree from Harvard Medical School in 1886. In 1917 he was appointed as director of orthopedic surgery for the Army. He was a former director of the Orthopedic General Hospital and was the first president of the

Boston School for Occupational Therapy. He was one of the founders of the Industrial School for Crippled and Deformed Children and at the time of his death was the editor of the *Journal of Bone and Joint Surgery*.

Dr. Brackett was a fellow of the Massachusetts Medical Society and the American Medical Association. He was also a member of the American Academy of Orthopaedic Surgeons and the American College of Surgeons.

His widow survives him.

LUCY — JOHN J. LUCY, M.D., of Boston, died December 28. He was in his forty-eighth year.

Born in Boston, he attended Boston College and received his degree from Harvard Medical School in 1920. He was assistant chief surgeon at the Boston City Hospital and was a staff member of the Cambridge Hospital. Dr. Lucy was a member of the Massachusetts Medical Society and the American Medical Association. He was also a fellow of the American College of Surgeons.

His widow, his mother and seven children survive him.

MACLEOD — HARRY F. MACLEOD, M.D., of Boston, died December 21. He was in his seventy-second year.

Dr. MacLeod received his degree from the University of Pennsylvania School of Medicine in 1894. He was a former member of the Massachusetts Medical Society.

A son survives him.

MALONE — CHARLES MALONE, M.D., of Jamaica Plain, died October 10. He was in his sixty-eighth year.

Dr. Malone received his degree from Tufts College Medical School in 1902 and since that time had practiced in Jamaica Plain. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

Two sons and a daughter survive him.

MANEY — JOHN J. MANEY, M.D., of Lawrence, died December 11. He was in his sixty-eighth year.

Dr. Maney graduated from Tufts College, and received his degree from Baltimore Medical College in 1900. He was a former member of the Massachusetts Medical Society.

A son, four brothers and three sisters survive him.

MISCELLANY

DOCTORS AT WAR

On December 26, the American Medical Association and the National Broadcasting Company, in official co-operation with the Medical Department, United States Army, and the Bureau of Medicine and Surgery, United States Navy, began the third series of the coast-to-coast radio broadcast, "Doctors at War," the current series being entitled "Doctors at War." These broadcasts will be continued for twenty-six consecutive weeks and are scheduled at 8:00 p.m. (EWT) on Saturday. They consist of short dramatizations that give a vivid picture of the work of physicians in the Army, in the Navy, in industry and at home.

CORRESPONDENCE

MASSACHUSETTS TUBERCULOSIS LEAGUE

To the Editor: In behalf of the Massachusetts Tuberculosis League I wish to express my appreciation for the

splendid editorial on the Christmas Seal Campaign in the December 10 issue of the *Journal*.

You may be interested to know, in connection with your statement that the seals, among other things, are partly "to provide x-ray equipment and other diagnostic facilities for kindred purposes," that the directors of the League voted to underwrite the purchase of a portable 4-by-5-inch photoröntgenographic unit for use in defense and other industrial plants and in high schools. The equipment mounted on a special motor truck will cost about \$14,000. Many of the affiliated branches of the League have already allocated 3 per cent of their 1943 Seal Campaign receipts toward the cost of this apparatus. It is to be hoped that all will contribute a like amount so that no more than \$5000 will have to be taken from the reserve fund.

Arrangements have been made to lend this unit to the Division of Tuberculosis of the Massachusetts Department of Public Health: they will operate it with their present personnel and will be responsible for its maintenance. This new type of film, because of its smaller size, costs only one tenth as much as the film in general use. It is therefore possible to x-ray many more persons without increasing the outlay for this best of all case-finding procedures. Under the plan men and women will receive the benefit of an examination that is now the privilege of those entering military service. Furthermore, to have the official and voluntary health agencies working in close harmony and pooling their resources to make more effective the attack on tuberculosis is a noteworthy achievement in co-operation.

HENRY D. CHADWICK, M.D., *President*
Massachusetts Tuberculosis League, Inc.

1148 Little Building
Boston

BOOK REVIEWS

Personality and Mental Illness: An essay in psychiatric diagnosis. By John Bowlby, M.D. 8°, cloth, 280 pp. New York: Emerson Books, Incorporated, 1942. \$2.75.

This book is well written, and the writer makes some perfectly good points. He believes that it is absurd to avoid the fact that the personality before the onset of overt mental disease is of great importance. He is also quite properly impressed with the relative futility of dividing off the psychoneuroses from the psychoses.

The attempt to rearrange classification and to catalogue specific and nonspecific traits that can be used in appraising a mentally ill patient is interesting. The difficulty, which is quite obvious to the author as well as to the reviewer, is that the theoretical discussion is not convincing without a vast amount of evidence, which certainly is not presented in this volume and which can hardly be supplied until large numbers of cases are watched over many years.

Skin Grafting from a Personal and Experimental Viewpoint. By Earl C. Padgett, M.D. 4°, cloth, 149 pp., with 65 illustrations and 3 tables. Springfield, Illinois: Charles C Thomas, 1942. \$4.50.

This book embodies the material of Dr. Padgett's clinical as well as experimental work. After a brief historical outline of the gradual progress of the methods of skin grafting during the span of a century and a half, the author discusses the interesting problem of homotransplantation and heterotransplantation methods. From his clinical as well as experimental evidence he concludes that

autotransplantation of skin usually succeeds; that syngenesiotransplantation of skin is theoretically improbable except in identical twins, in whom it is theoretically probable and has been accomplished clinically; and that, for all practical purposes, homotransplantation of skin may be relegated to the realms of medical mythology.

The author next considers methods of cutting skin grafts, and emphasizes the superiority of the dermatome, especially when it is necessary to remove a large piece of skin of uniform thickness. There is no doubt that this instrument, introduced to the profession by the author, has filled a great need and has contributed a good deal to the progress of skin grafting. However, in the opinion of the reviewer, the time-honored method of using a razor-edge knife still has its place, especially when a very thin skin graft or grafts of small size are needed.

Dr. Padgett discusses the relative merits of pedicle grafts and their indication as compared with skin grafts, and properly emphasizes the importance of well-conceived and well-planned pedicle grafts.

The book is printed on coated stock, with many photographs and illustrations of different cases. There are several statistical tables.

Although the literature of skin grafting is abundant in medical periodicals and books, this small volume will undoubtedly occupy a place in the library of those who are particularly interested in traumatic surgery.

Pediatric Gynecology. By Goodrich C. Schauffler, M.D. 8°, cloth, 384 pp., with 66 illustrations. Chicago: The Year Book Publishers, Incorporated, 1942. \$5.00.

The dust wrapper of this book carries the words "a pioneer book by a pioneer worker." They are true words. There exists no other book, the reviewer is quite sure, that covers the ground of this one. Most pediatricians surely and gynecologists probably know very little indeed about the disorders of the immature female genitalia. With the power to make correct diagnoses they would probably have difficulty in deciding how to treat even halfway adequately.

This treatise supplies a good many of the inadequacies in this knowledge. The author furnishes an abundance of concrete facts, and his conclusions concerning treatment and method of approach — for in such a field, tact and delicacy as well as judgment are of the highest importance — have the earmarks of practicality and good common sense. His technics, it is true, come far more naturally to the gynecologist than to the pediatrician. To the latter, indeed, the greatest value of the book is in teaching him when to look to the former for assistance, what that assistance should be and what may be expected from it. The book steps over even into urologic, proctoscopic and medicolegal fields.

It is an original book and an important book, which is highly recommended.

From Infancy through Childhood. By Louis W. Sauer, M.D., Ph.D. 12°, cloth, 200 pp., with 13 illustrations and 5 charts. New York: Harper and Brothers, 1942. \$2.00.

This is another manual for home consumption on the care and management of infants and children. The author is a pediatrician of experience and a safe and sane guide in such matters; moreover, his advice is brief and clear. The wonder arises, however, why author or publisher should have deemed worthwhile this excursion into a field already so well covered: there are books and books on the subject, all of which, in essence, repeat the same things. And this is just one more.

(Notices on page x)

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THE HISTORY OF THE DISCOVERY AND ISOLATION OF THE MALE HORMONE

GERRARD J. NEWERLA, MD

ALBANY, NEW YORK

THE first knowledge of testicular function was acquired empirically by the ancients when domestic animals were castrated for various reasons. However, the specific effects in men were also familiar to those early civilizations where eunuchs were a part of the social order. Furthermore, the *Ayurveda*, by Susruta of India,¹ written about 1400 B.C., recommended the administration of testicular tissues for the cure of impotence. From these times until within the past twenty years, with the exception of very few animal experiments in the middle of the eighteenth and nineteenth centuries, the knowledge of the secondary functions of the gonads did not advance much beyond the facts known in the Middle Ages.

With some degree of overlapping, the investigation of the endocrine functions of the testes may be grouped with a certain fitness into the following periods: speculative and observational; experimental; and analytic and synthetic.

SPECULATIVE AND OBSERVATIONAL PERIOD

The customs of primitive people and society until rather recent times dictated forms of organo-therapy and the use of organs as medicine, such as the eating of hearts from animals, or even from man, to encourage bravery, or the use of brain as food to counteract idiocy. Perhaps it was for such reasons that the ancients and the people of the Dark Ages indulged in organo-therapy, especially of such substances as bile, blood, bones, dung, brains, feathers, horns, intestine, placenta, reproductive organs and teeth. Often the difficulty of obtaining a part was its most attractive attribute. Nothing was too disreputable for use. *Dieck Apotheken* specialized in secretions and excretions,² but other books, especially Heberden's³ *Antitheriaca* (1745), discredited these disgusting preparations. It is interesting to note that today many of the sex hormones, including that of

the male, are obtained from human waste products.

The type of therapy employed by medieval physicians is an indication of their conception of the nature and cause of disease. At a time when disease was treated according to a jumble of mysticism, philosophy and dogma, critically appraised concepts of the action of even the exocrine glands could not be formulated. There are some physiologic statements which in the light of modern knowledge show glimpses of suspected fact. A vague foreshadowing of the endocrine function of the testis can be found in the works of Aretaeus,² the Cappadocian (ca 150 A.D.), in the chapter on gonorrhea: "For it is the semen, when possessed of vitality, which makes us to be men, hot, well braced in limbs, well voiced, spirited, strong to think and act. For when the semen is not possessed of its vitality, persons become shrivelled, have a sharp tone of voice, lose their hair and their beard, and become effeminate, as the characteristics of eunuchs prove." Rolleston⁴ mentioned that Johannes Mesue, the Elder (777-837), prescribed testicular extracts as an aphrodisiac and against pulmonary tuberculosis. Some real understanding of the problem was first voiced in 1775 by Théophile de Bordeu, a graduate from Montpellier and a physician at the court of Louis XV. He was the founder of the theory of vitilism, and strove to show that the humoral pathology of Hippocrates was due to bodily secretions. For many organs and their secretions he enumerated specific diseases. In this manner he arrived at the concept that each organ of the body produces a substance which enters the blood stream and that the sum total of these forces regulates bodily functions. He even cited the well recognized underdevelopment of secondary sexual characteristics in eunuchs, capons and spayed female animals in connection with the absence from the blood of specific secretions of the gonads. In his book, *The Medical Analysis of Blood*, he⁵ came to the con-

clusion that "each [of these organs] is a store room and laboratory for a particular humor [substance] which is given off into the blood after it has been prepared in its bosom [that is, the organ], and has thus conferred upon it [the humor] a radical [specific] character."

These views are very similar to those expressed by Brown-Séquard,⁶ and are practically identical with the modern definition of endocrine function. Speaking of testicular secretions, de Bordeu⁷ stated: "I accept as fully demonstrated medically the view of such continuous emanations from each organ into the blood. And if we take into consideration the facts discovered by anatomists with regard to the existence of the lymphatics, I would say that the gelatinous liquor [that is, the semen of the testis] is sent into every organ of the body by certain vessels, and confers upon the chyle in the thoracic duct the properties and peculiarities of the 'ingredients' of which they are composed." He believed that the gross structure of the cellular tissue was the chief site of exchange of these secretions, since the true dimensions of the lymphatic network were still incompletely known. No one prior to Berthold,⁸ or even Brown-Séquard, visualized as closely as did de Bordeu the true mode of action of the endocrine glands. Neuburger⁹ in 1911 emphasized the approximation of de Bordeu's speculation to the mechanism of internal secretions by ductless glands. Yet others consider the uncritical writings of de Bordeu as an attempt to classify cachexias resulting from various secretions, excretions and organs in a none too discerning fashion. Garrison,¹⁰ in the "History of Endocrinology," writes: "The book is a typical example of the purely theoretical reasoning so common in the medical literature of the eighteenth century, in which an intolerable deal of verbiage is spread over the smallest substructure of fact." He regarded the sexual secretions as giving "a male—or female—tonality" to the organism, "setting the seal upon the animalism of the individual." Observations regarding castration, known to animal-breeders since much earlier times, were confused by him with hearsay reports and anecdotes, and did not induce him to test his ideas experimentally. The historian must remain on guard so as not to read modern concepts into fanciful hypotheses.

During this period of speculation, some progress was made in the study of the anatomy and physiology of the ductless glands. Aristotle, in his *Historia Animalium*, written prior to 300 B.C., described the testes and ovaries in many species of animals and showed a clear conception of the effect of castration. In book nine of the fourth volume he¹¹ wrote: "If the bird be full-grown [when castrated] his crest grows fallow, he ceases

to crow, and foregoes sexual passion; but if you cauterize [that is, castrate with hot irons] the bird when young, none of these male attributes or propensities will come to him as he grows up. The case is the same with men; if you mutilate them in boyhood, the later-growing hair never comes, and the voice never changes but remains high-pitched; if they be mutilated in early manhood, the late growths of hair quit them except the growth in the groin, and that diminishes. . . ."

While the knowledge of secretions of the testes, other than the semen, gradually evolved, the study of glands in general, and of the ductless glands in particular, formulated many fundamental principles that applied to all internal secretions. Galen knew of the existence of the pituitary gland, although Vesalius¹² described it first in 1543 and named it after the Latin word *pituita*, meaning "mucus" or "phlegm,"—which, as both believed, was secreted by it. Schneider¹³ in 1655 and Lower¹⁴ in 1670 proved that such mucus did not pass from the brain to the nose, and suggested an internal secretion of this gland. Willis¹⁵ in 1664, according to Rolleston,¹⁶ believed that "the blood poured out something—through the spermatic arteries to the genitalia—and that it received in turn certain ferments from these parts,—that is, certain particles imbued with a seminal tincture and carried back to the blood,—which makes it vigorous and instills into it a new and lively virtue."

Gley¹⁷ claimed that Legallois¹⁸ in 1801 had come more closely to the concept of internal secretion than had de Bordeu. Legallois found that although arterial blood was of the same composition throughout the body, venous blood varied considerably, depending on the site from which it was obtained. This difference he attributed to the fact that the organs removed something from the blood, which then passed into the veins. This claim is scarcely as impressive as that of Willis and of Lower.

Thus, in less than half a century, ductless glands were recognized as closely allied to the vascular system and capable of secreting a substance into the blood stream. The close association with the blood vessels was pointed out by Broussais¹⁹ in 1817 for the spleen and the adrenal, thyroid and thymus glands, and by Béclard²⁰ in 1823 for the pituitary and pineal glands. Johannes Mueller²¹ in 1834 and Henle²² in 1841 differentiated between glands with and without ducts, and believed that the ductless glands changed the composition of the blood.

One may say that ancient and medieval scientists formulated certain philosophical theories on glandular secretions. These hypotheses, when read

from a modern point of view, seem to indicate in many instances a fair comprehension of the presence and function of the endocrine secretions, especially those of the testis. Such an assumption, however, is pure inference, and these concepts may not have been so clearly formulated in the minds of the philosophers, who based their conclusions on a few casual observations.

EXPERIMENTAL PERIOD

Many centuries had passed since Aristotle ascribed pubertal changes to the function of the gonads, as such manifestations were absent in castrates. In the era of enlightenment, objective study was combined with sound reasoning by many anatomists and scientists, until John Hunter and Berthold approached the problem experimentally. John Hunter²³ in 1762 attempted to ascertain whether the genital organs of one sex could be grafted to and grow in the body of the opposite sex. He transplanted the testicles of a cock into the abdomen of a hen, and in several cases found that some grafts had taken root there, but "did not come to perfection." For this reason he considered the experiments as incomplete and of no value. However, he failed to mention any "masculinization" effects observed with the few successful transplants.

In 1848, Berthold,⁸ then professor of physiology in Göttingen, removed the testes of four roosters and replaced one testis in an unusual abdominal position in each of two capons. He killed these two capons six months later, and found that because of the testicular grafts "these animals remained male in regard to voice, reproduction instinct, fighting spirit, and growth of comb and wattle. . . . The consensus [that is, the interrelation of function among different parts of the body] is maintained by the productive influence of the testicle; that is to say, by its effect upon the blood, and through the blood, upon the organism."

Berthold's clear and important demonstration of endocrine secretion was published in a five-page paper which remains the only noteworthy epitaph of an author who wrote voluminously on other subjects. Rudolf Wagner,²⁴ the physiologist, could not confirm Berthold's findings in 1850, and the influence of the discovery was almost forgotten until Biedl,²⁵ in his monograph, *The Internal Secretions*, resurrected the work and bestowed on Berthold "the honor of having first proved the existence of an 'internal secretion' and of having recognized its significance."

By 1850 the long-recognized influence of the testis had been demonstrated to be caused by blood-borne secretions of these ductless glands. These facts were disregarded, however, and it was

only after impressive experiments in the field of metabolism that inferences were drawn regarding endocrine organs. Great progress followed the work of Claude Bernard,²⁶ who in 1843 proved that cane sugar is changed to dextrose by gastric juice. These results became widely known, and as Garrison²⁷ remarks regarding internal secretions, "It was the fact that glycogen [Bernard's *sécrétion interne* of the liver] could be seen, touched, tasted and experimented upon, as such, that established the theory of internal secretions as a working principle in physiology."

At the time of Bernard's studies, Thomas Addison²⁸ extended to the adrenal gland the principle of glandular hypofunction, which had been recognized for centuries with regard to the testes, but had not been known to apply to the other glands. His classic description of the disease of the adrenal glands that now bears his name was verified within a year by Brown-Séquard,²⁹ who extirpated the adrenal glands and found that the animals showed the symptoms described by Addison.

The latter part of the nineteenth and the early part of the twentieth century was a period in which general principles were outlined. Bernard had formulated the concept, *la fixité du milieu intérieur*, or the constancy of the internal environment, by which he meant that higher animals maintained a constancy of temperature and bodily fluids. It became known that the endocrine system, in conjunction with the nervous system, especially with the autonomic portion, aided greatly in maintaining the remarkably even tenure of involuntary bodily activities.

A slight digression is in order for the purpose of tracing the development of the fundamental nomenclature of endocrine secretions. According to Rolleston,³⁰ the term "internal secretion" was first used by Claude Bernard in a lecture at the Collège de France on January 9, 1855. Speaking of his work in glycogenesis, Bernard said that the liver had an "external secretion" of bile and an "internal secretion" of sugar, which passes directly into the general circulation.

Bayliss and Starling,³¹ in 1903, believed that the term "internal secretion" inadequately expressed the widespread action on the body as a whole of chemical entities produced in certain organs, and transported elsewhere by the blood and the lymphatics. Starling,³² in the first Croonian Lecture before the Royal College of Physicians, on June 20, 1905, spoke of "the chemical messengers or 'hormones' [I excite or arouse]." According to Rolleston³³ this word was suggested by W. B. Hardy after consultation with W. T. Vesey from Caius College, Cambridge.

In the early years the selection of the term "hormone" was frequently criticized on the ground that it applied by definition only to substances that have a stimulating action, and failed to include those that had an inhibiting or depressing effect. Yet Jayle³¹ stated that this word or its derivatives had already been used by Hippocrates. Likewise John Smith,³² a physician from Brasenose College, Oxford, used it in his *Gaerokomia Basilikae*, when he spoke of the "hormetick power and concentration" of the muscles. Schäfer,³³ in his book, *Endocrine Organs*, suggested the term "hermone" (from Hermes, "messenger"), which would exclude any ambiguity and could be applied to both stimulating and depressing agents. In 1913, he³⁷ had already advanced the term "chalone" ("I loosen") for the inhibitory hormones and the word "autocoid" ("self-remedy") as a generic name for all internal secretions, and reserved the noun "hormone" exclusively for stimulating agents. The use of these terms, however, did not become popular, and is at present largely discontinued.

Pende,³⁸ an Italian, had introduced the term "endocrinology" ("I separate within") in 1909, while Gley,³⁹ a Frenchman, suggested the term "harmazone" ("I regulate") for the morphogenetic and growth-controlling secretions of the gonads and thyroid and pituitary glands at the International Congress of Medicine in London in 1913. The word "parahormone" was chosen to denote metabolic products, such as carbon dioxide, which act like hormones at a distant site.

Ironically, after a period of brilliant experimentation, clinical endocrinology was introduced by the uncontrolled study and blatant claims for rejuvenation in 1889 by Brown-Séquard,⁶ who at the age of seventy-two injected himself with aqueous extracts of the testes. He claimed as results an improvement in general health, muscular strength and appetite, and regulation of the intestinal tract and mental faculties. He⁴⁰ even suggested orchitic extracts as a panacea and advised their use, for example, in *tabes dorsalis*.

Preparation and critical investigation of extracts were logical steps in this practical period of endocrinology, and Brown-Séquard's statement of the principles involved was essentially correct. Garrison⁴¹ summarizes Brown-Séquard's ideas as follows:

All the tissues, in our view, are modifiers of the blood by means of an internal secretion taken from them by the venous blood. From this we are forced to the conclusion that, if subcutaneous injections of the liquids drawn from these tissues are ineffectual, then we should inject some of the venous blood supplying these parts. . . . We admit that each tissue, and more generally, each cell of the organism, secretes on its own

account certain products or special ferments, which, through this medium, influence all other cells of the body, a definite solidarity thus being established among all the cells through a mechanism other than the nervous system. . . . All the tissues [glands or other organs] have thus a special internal secretion and so give the blood something more than waste products of metabolism. The internal secretions, whether by direct favorable influence, or whether through the hindrances of deleterious processes, seem to be of great utility in maintaining the organism in its normal state.

This is the theory of de Bordeu, restated at a stage in the development of science when accrued knowledge permitted more precise formulation. The preceding quotation shows beyond doubt that Brown-Séquard clearly believed that the endocrine glands liberate active substances into the blood stream. This passage is markedly different from his views in 1855, when he²⁹ stated that extirpation of the adrenal glands permitted accumulation of pigments in the blood, these pigments becoming poisonous in the absence of detoxification by the glands.

The unfortunate parts of Brown-Séquard's work were the uncritical manner of investigation and the extravagant claims of rejuvenation. With the possible exception of the search of Ponce de Leon, the ageless quest for perpetual youth was never brought so closely and so attractively to the attention of the world. The limitations in the technics of grafting of the testes and in administration of testicular extracts were overlooked. Much of his so-called therapy was useless and unapproved by competent contemporaries or successors of Brown-Séquard. The susceptibility of many minds in matters pertaining to sex and the false hopes raised by extravagant claims led inevitably in a pendulum fashion to a viewpoint strongly antagonistic to the acceptance of the efficacy of any testicular substances, an opinion well warranted until the last few years. Early experiences with inactive ovarian mushes and dried matter increased the skepticism concerning the usefulness of gonadal preparations (Novak⁴²). The inevitable result was that strong prejudice for and against a mode of therapy has been built not on controlled observation and experimentation, but on wishful conclusions, inactive preparations and useless grafting operations. When active chemical substances of known, measurable and stable potency were prepared in 1936, there was already a great superstructure of largely discrediting data purportedly related to the method of substitution therapy, but in actuality proving not that the principle is incorrect, but that the technics previously utilized in substitution therapy were inadequate. This distinction must be made between the use in human beings of testicular grafts or extracts in contrast to

the present-day employment of crystalline compounds.

The unsavory aroma of attempts at rejuvenation did not prevent rapid advances in clinical endocrinology. It is interesting to speculate on the course of events had Brown-Séquard tried his theory of *autotherapy in hypothyroidism* instead of in attempted rejuvenation. Yet his work in attracting world-wide attention encouraged trial of substitution therapy in states of deficiency resulting from the poor functioning of other glands.

Overactivity of the endocrine glands, by the nature of the phenomena involved, was a matter appreciated more slowly than were deficiencies in glandular activities. The testis, the gland in which hypoactivity and endocrine secretion were first demonstrated, is not known to produce any striking sequelae of hyperactivity. Precocious sexual development is occasionally seen with interstitial tumors of children, but the condition of masculinity is not known to exceed the stage seen in normal men.

Although principles were formulated and rapid progress made in investigation of other endocrine glands, the study of testicular function advanced slowly, and on many fronts there was only a marking of time. Interrelations with other glands, particularly with the pituitary, were clearly demonstrated by studies of these glands, notably in the work of Rathke,⁴³ Frölich,⁴⁴ Cushing,⁴⁵ Evans⁴⁶ and Smith.⁴⁷

In 1908-1910, some of the details of the castrate condition in men were supplied by Tandler and Grosz⁴⁸ in a series of studies of the Skoptsy, a religious sect whose members inflicted self-mutilation according to the following advocacy in the Bible:

For there are some eunuchs, which were so born from their mother's womb: and there are some eunuchs, which were made eunuchs of men: and there be eunuchs, which have made themselves eunuchs for the kingdom of heaven's sake. He that is able to receive it, let him receive it. (Matthew xix:12.)

Additional and significant data concerning the action of male hormone substances were gleaned by animal experimentation with grafting and other manipulation of the testes (Lipschütz⁴⁹), but unhappily some studies bore the connotation of rejuvenation. A history of research of male-hormone substances would be incomplete without some mention of attempts at rejuvenation.

A chief drawback to the accomplishment of rejuvenation lies in the fact that aging affects the structure and function of cells in a manner not reversible by sex hormones. Not all cells can be expected to be restored to a status compatible with an earlier age. The use of the term "rejuvenation"

(Steinach⁵⁰) deserves severe indictment, even if applied solely to the genital organs, for the changes induced by androgenic stimulation are scarcely a "re-establishment of youthfulness." It is of fundamental importance to realize that aging occurs in various degrees in different cells, and only wishful thinking can glibly circumvent the obstacles opposing any rejuvenation merely by secretions of the testicle, even if the secretions resemble those existent when the individual was younger. It is not inappropriate to recall that in the immature boy, youth prevails without the prodding of large amounts of testicular secretions.

To those with scientific inquiry were added searchers, not of facts, but for means whereby the testis would become the fountain of youth. Charlatans reaped a financial windfall. The chief methods employed to obtain testicular secretions were implantations of a testis from another man or beast, the injection of extracts from animal testes and the stimulation to secretion of the testes already existing.

Transplantations of the testis involve a number of problems, especially satisfactory vascularization and compatibility with the environment provided by the host. Despite any excellency of operative methods, it is held in some quarters to be almost axiomatic that grafting in mammals should be to a host of the same species. Testes from goats, monkeys or other animals have not proved to have satisfactory survival and function after transplantation to man. Persistence of a mass of tissue at the site of implantation is in itself not assurance that the graft has "taken," for microscopic examination may reveal only fibrous tissue remaining. Even within the same species successful grafting is enhanced by inbreeding. Although many transplants of testes have been made from one man to another, the results have been poor, a fact not astounding in view of the difficulties of obtaining specimens in good condition, a sufficiently close relation between donor and host and a suitable endocrine status in the host. Some of the men receiving grafts have been eunuchoids in whom gonadotropins may have failed to stimulate the individual's own testes and in whom the pituitary rather than the testes have been primarily responsible for the eunuchoidism. From the standpoint of reproductive purposes, it should be noted that even if interstitial elements in the graft were to persist, the seminal epithelium would be less likely to grow satisfactorily.

Attempts to stimulate the testes of an individual can be accomplished in certain cases by the administration of gonadotropic substance. Claims have also been advanced, but without general acceptance, that testicular secretions can be augmented

by ligation or resection of the vas deferens. The theoretical basis of such operations is that the interstitial tissue is the source of androgens; that blocking of the seminal duct near the testis causes destruction of the seminiferous epithelium, presumably because of pressure; and that when the seminal epithelium is destroyed there is an increase in interstitial cells, and therefore more hormone is produced.

The period of experimentation occupied about a century and a half. Work, at first sporadic and haphazard, progressed slowly and was often misinterpreted. Berthold, about one hundred years ago, conducted experiments under the strictest control, the significance of which was fundamental and is still unimpeachable. However, the blatant claims of Brown-Séquard discouraged further advances, even though the extracts produced by him may be considered as the first attempts to isolate the male hormones. Subsequent workers advanced the knowledge of endocrinology as a whole and devised a fundamental terminology. However, the unwarranted claims of rejuvenation propounded by Steinach and by Voronoff as results of testicular grafts had the same effect as the claims of Brown-Séquard had on the studies of Berthold.

ANALYTIC AND SYNTHETIC PERIOD

Progress in the preparation of testicular-hormone extracts was slow. The lack of suitable methods for assay and the absence of adequate resources for male-hormone substances became evident, especially when compared with the high titers of female hormone found in the urine of pregnant women and domestic animals. The numerous experiments of earlier investigators indicated at least one testicular hormone, but efforts to isolate it remained futile for many years.

The discovery by Pézard⁵¹ in 1911 of the capon as a quantitative biological test animal for androgens was a fundamental step forward. Pézard injected extracts from the testes of crypt-orchid pigs twice weekly for five months into a cockerel that had been castrated two months earlier and showed castration atrophy, and found that one tenth of a cryptorchid hog testis would produce an increase in the size of the comb and the wattle of this capon as compared with similar control birds. However, the omission of detail in his report prevented repetition and confirmation of his experiments.

McGee,⁵² in 1926, working in the laboratory of Koch in Chicago for his doctor's dissertation, was the first to prepare a lipoid extract from fresh bull's testes, 0.01 mg. of which would restore the atrophic comb of a capon. He thus confirmed an endocrine function of the testis. Three years

later Loewe and Voss,⁵³ of Mannheim, reported before the Academy of Sciences in Vienna that an extract obtained from 3.6 liters of urine from normal men would restore the castration effects of the seminal vesicles of a mouse.

Moore and his collaborators,⁵⁴⁻⁵⁸ of Chicago, in a series of studies, investigated for many years the physiologic action of testicular extracts, and not only defined the rat unit but also performed tests on spermatozoon motility, on electric ejaculation in guinea pigs and on the cytology of the prostate, the seminal vesicles and the vas deferens of the rat. Heller,⁵⁹ in 1930, studied the effects on Cowper's gland, and Binet and Luxembourg,⁶⁰ of Paris, in 1939 found that the female Xiphophore, an aquarium fish, produced a characteristic male caudal fin when injected with male urine twice weekly for six weeks. Moore and Price,⁶¹ in a classic study, presented the most adequate exposition of the interrelations between the anterior-pituitary gland and the testes.

During these years progress was rapid. In 1931, Butenandt,⁶² of Danzig, succeeded in isolating in crystalline form 15 mg. of two chemically pure substances, "androsterone" and "dehydroandrosterone," from 15,000 liters of male urine by the Funk-Harrow⁶³ method. He found that these substances were sterols of the probable formulas, $C_{16}H_{26}O_2$ or $C_{19}H_{30}O_2$, and that they were closely related to the female hormone "estrone." Ruzicka and his associates,⁶⁴ at the Polytechnic Institute in Zurich, were impressed by the similarity of Butenandt's formula for androsterone to that of cholesterol. They attempted to produce, and promptly succeeded in doing so, a synthetic crystalline compound of the same formula as Butenandt's androsterone. They evolved the process which is now used for the commercial synthesis of androsterone and testosterone by the degradation and hydrogenation of epicholesterol.

At about the same time, chemists were engaged in the laboratory of Laqueur in Amsterdam in similar work. In 1935, David et al.⁶⁵ announced the isolation of a crystalline substance, "testosterone," from bull's testes, just before Ruzicka's laboratory⁶⁶ synthesized it. This testosterone was many times more potent than the androsterone of Butenandt, and differed from it chemically by the reduction of the keto radical at carbon atom 17. Up to the present time more than thirty substances of male-hormone character, but of different degrees of physiologic activity, have been prepared synthetically by the degradation of sterols. Essentially there are two types, a saturated and an unsaturated series. Koch,^{67, 68} in 1937 and in 1939, has given the most comprehensive exposition of the chemistry of these androgenic substances. The

following excerpt will best convey the chemistry involved:

A consideration of androsterone and its closest isomers . . . shows that the *cis* configuration of the OH on carbon atom 3 with reference to the H on carbon 5 is very important providing the H on carbon 5 is *trans* to CH₃ on carbon 10. If the H on carbon 5 is *cis* to the CH₃ on carbon 10, as it is in the derivatives from coprosterol and epi-coprosterol, the physiological activity is negligible. The importance of the configuration about carbon 3 is again shown when the 17-keto group is reduced as in the androstanediols. Note that reduction of the 17-keto group in androsterone and *trans*-androsterone (dehydro-iso-androsterone) increases the potency. In other words, the 17-position secondary alcohol group is even more important than the 3-epi-OH (3-*trans*-OH) form in determining potency. If both 3 and 17 positions are oxidized to ketones, as in androstanedione, there is not much change from the androsterone potency.

The discussion above covers the saturated series. In the unsaturated series the conversion of the 17-keto group into a secondary alcohol may alter the activity slightly, but not as much as in the saturated series. . . . Comparison of the unsaturated with the saturated di-ketones does not reveal a striking effect unless the unsaturated group is between carbons 1 and 2; then the unsaturation produces a striking loss of potency. . . . Conversion of carbon 17 into a tertiary alcohol with the -OH kept *trans* also increases the potency somewhat. It appears then that the most favorable arrangements for high potency known thus far are found in testosterone and 17-methyl (*cis*) testosterone.⁶⁸

Male hormones and their derivatives are therefore sterols related to those found in the bile acids, adrenal cortex, cardiac glucosides and the digitalis sapogenins. They are closely related to some vitamins and to the carcinogens. Androgenic substances have been isolated from urine, feces and the adrenal glands. The urine of normal men and women contains androsterone and dehydro-iso-androsterone (Tscherning⁶⁹ and Butenandt and Tscherning⁷⁰) in rather large quantities as compared with the low titers found in the tissues.

Although male hormone was isolated and synthesized in a comparatively short time, there was not such progress in the determination of its sources in the testicle. The interstitial cells, first described in 1850 by Leydig,⁷¹ then professor of histology at Würzburg, and since identified by his name, are commonly believed to be the elements that produce this hormone. This view was first advanced in 1896 by Reinke,⁷² who described certain crystalloids in these cells, now known as the "Reinke crystalloids." Ance! and Bouin⁷³ from 1903 on devoted numerous papers to the study of these cells. They introduced the term "interstitial gland" to denote the secretory function of these cells, and argued strongly in favor of their being the source of male hormone. Steinach,⁶⁹ in 1912,

coined the name "puberty gland"; he⁷⁴ believed that it not only secreted the androgens, but could also be rejuvenated by vasoligation, a concept which became very popular for many years. Bouin,⁷⁶ in 1931, advanced additional evidence to prove that the interstitial cells were the producers of the testicular hormone.

This hypothesis, however, has been greatly contested, and is still not generally accepted. Furthermore, McCullagh, alone⁷⁶ in 1932 and with his associates⁷⁷ in 1935, presented some evidence that the testis may also secrete a second hormone, "inhibin," which inhibits the activity of the pituitary gland. Although the presence of the inhibin principle has been denied by some authorities, there still remains some good evidence in its favor. However, further experimental studies are needed to settle this question, which is mentioned here merely for its historical interest.

* * *

In conclusion, it can be stated that the testis was the organ first suspected of, and associated with, an internal secretion. It was likewise the first gland subjected to animal experimentation. Yet, in spite of this, approximately a century—from 1848 until 1935—was needed before the androgenic hormone was isolated and synthesized in pure crystalline form. This fact is still more surprising when comparison is made with the internal secretions of other glands, such as the thyroid, the parathyroid, the pancreas and the adrenals, whose endocrine activity was not suspected until much later, yet whose active principles were isolated chemically, and even synthesized, much earlier than were those of the testis.

With the chemical isolation and synthesis of the androgens a period has been reached in which they are studied in relation to the general metabolism of the body and to the other endocrine glands, especially the pituitary and the adrenal cortex, and in which they are applied therapeutically in several clinical syndromes. This work already commands a huge literature, but concepts are still indefinite and need more study to permit final conclusions.

In order to recapitulate the history of the discovery and isolation of male hormone, it is appropriate to present the high lights of this interesting chapter of endocrinology in a chronological tabulation:

- 1400 B. C. The *Ayurveda* of Susruta recommends testis tissue as treatment for impotence.
- 460-370 Hippocrates uses the word "hormone" for certain ferments.
- 384-322 Aristotle describes castration effects in birds, beast and man.

- 40 A.D. Matthew mentions in his Gospel eunuchs made by God (congenital) and by man (castrated), and thus furnishes the basis for the self-mutilation of the Skopets sect of Russia.
- 150 Aretaeus, the Cappadocean, in his description of gonorrhea suggests that the semen is the basis of the characteristics of the male.
- 131-201 Galen of Pergamus knows of the pituitary and believes that it secretes a "phlegm" into the nose.
- 777-837 Johannes Mesuë, the Elder, prescribes testicular extract as an aphrodisiac.
- 1543 Vesalius describes the anatomy of the pituitary gland and coins its present name.
- 1664 Willis believes that the blood receives certain ferments from the spermatic veins that make it vigorous and lively.
- 1666 John Smith uses the word "hormetick" for certain muscular metabolic products.
- 1745 Heberden's *Antitheriaka* leads to the purification of the "filth" pharmacopocias.
- 1762 John Hunter transplants the gonads of one sex into the other sex, but his experiments are not successful.
- 1775 Théophile de Bordeu argues in favor of internal secretions from some glands.
- 1801 Legallois finds that venous blood varies according to the organs from which it comes.
- 1817 Broussais points to the close association of blood vessels with the adrenal, thyroid and thymus glands and the spleen.
- 1823 Béclard shows the close relations of blood vessels to the pituitary gland and the pineal body.
- 1834 Johannes Mueller differentiates between glands with and without excretory ducts.
- 1843 Claude Bernard demonstrates glycogenesis and glycogenolysis as functions of the liver.
- 1848 Arnold Berthold performs the first successful testicular transplants in capons and thus proves an endocrine function of the testes.
- 1850 Franz von Leydig describes certain cells in the testis, which are now known as the "Leydig interstitial cells."
- 1855 Thomas Addison publishes his classic monograph on adrenal disease, known now by his name.
Claude Bernard introduces the term "internal secretion."
- 1889 Brown-Séquard publishes his famous paper on self-rejuvenation after treatment with testicular extracts.
- 1896 Reinke describes the crystalloids of the interstitial cells, now bearing his name, and suggests that these cells secrete the male substances.
- 1903 Ancel and Bouin introduce the term "interstitial gland" to indicate the secretory function of the interstitial cells.
- 1905 Starling introduces the term "hormone" for all internal secretions, as known today.
- 1907 Tandler and Grosz describe the skeletal changes found in eunuchs and Skopets after pre-pubertal castration or self-mutilation.
- 1909 Pende introduces the term "endocrinology" for the science of internal secretions.
- 1911 Pézard discovers the capon comb and wattle growth as a test for male-hormone determination.
- 1912 Steinach coins the word "puberty gland" and suggests that it can be rejuvenated by ligation of the vas deferens, a procedure now known as the "Steinach operation."
- 1926 McGee produces a lipoid extract from bull's testes.
- 1929 Loewe and Voss produce an androgenic extract from urine.
- 1931 Butenandt isolates crystalline androsterone and dehydroandrosterone from male urine.
- 1934 Ruzicka and his assistants synthesize androsterone, and later also testosterone.
- 1935 David and his associates, in Laqueur's laboratory, isolate crystalline testosterone from bull's testes.

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MILITARY DISCHARGE FOR INADEQUACY*

Report of 182 Cases

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CAMP BLANDING, FLORIDA

MEDICINE is not yet an exact science. Army induction boards labor under difficulties that frequently increase the margin of error. They are compelled to work under great pressure, the time allotted is sadly inadequate, and there is often a shortage of trained specialists.¹ Moreover, it is impossible in one examination to weed out all those physically and psychically unable to perform as soldiers. Thus, unqualified men are occasionally placed in uniform. Unfortunately, this does not make them soldiers.

Army regulations provide for the discharge from the Service of these unfit persons. Those who fail because of organic disease or from psychoneurosis or psychosis are released under regulations providing for a certificate of disability for discharge.² This procedure we have outlined elsewhere.³

Under further regulations (so-called "Section VIII cases"),⁴ "when an enlisted man (1) is inept, or (2) does not possess the required degree of adaptability for military service, or (3) gives evidence of traits of character or habits which serve to render his retention in the service undesirable, or (4) is disqualified for service physically or in character, through his own misconduct," steps are taken to separate him from the service. This is not done, however, "until every reasonable effort has been made to develop the enlisted man concerned into a soldier." Further, every consideration must be given to the advisability of transferring the enlisted man to another organization of the regiment or post in order that he be given every opportunity to develop into a soldier. This does not apply to enlisted men who show undesirable habits or traits of character.

In most cases the discharge given is the "blue" discharge from the Army of the United States. This is neither honorable nor dishonorable; it is a discharge without honor. Exceptionally, an honorable discharge is given when the conduct of the enlisted man during his enlistment has been such as would render his retention in the service desirable were it not for his inaptitude or lack of required aptitude for military service. In these cases the certificate must show that retention is warranted. No discharge papers may be given for the reason for the discharge.

We have collected all these discharges, issued through the Station Hospital at Camp Blanding, Florida, for its first year, from November 5, 1940, to November 5, 1941.

The military personnel of this camp consisted of two divisions, the Thirty-First or Dixie Division, made up of troops from Florida, Louisiana, Mississippi, Alabama and Georgia, and the Forty-Third or New England Division, made up of troops from Maine, New Hampshire, Vermont, Rhode Island, Connecticut and Massachusetts, the Seventy-Fourth Field Artillery Brigade, composed of National Guard units from Georgia and New Hampshire and of men from the Regular Army, and the Corps Area Service Command troops from varied sources. The average camp population, subject to marked fluctuation, was approximately 30,000, ranging as high as 45,000 and at times dropping as low as 5000.

The total number of men discharged for inadequacy was 182. On the basis of an average camp population of 30,000 this is 0.6 per cent.

The following factors entered into the making of these decisions and must be considered in the appraisal of the statistics. The first factor is the difficulty in making many officers newly on active duty conform strictly to the necessary tedium of Army regulations; for this reason, many such cases have been overlooked. The second factor is the probability that many of these cases have been diagnosed as being due to organic disease. Too many physicians still refuse to recognize the frailty of the psyche because of overconcentration on the weakness of the soma. "If a man says he has a pain, how can you know he hasn't a pain?" Undoubtedly many diagnoses of sacroiliac sprain, mild heart disease, enuresis, flat feet, spastic colon and similar diseases should have been included in this group. And, finally, the board which must recommend discharge is composed of officers from the enlisted man's own company. Too often in National Guard divisions they have known the soldier at home. They are therefore inclined to doubt that he is a psychiatric case, or if they accept the diagnosis, they may be reluctant for personal reasons to discharge him on this ground. For all these reasons we believe that the number of discharges mentioned above is far below the actual number of cases warranting such action.

*From the
†Neuropsychiatry
‡Registrar, S

up Blanding, Fla.
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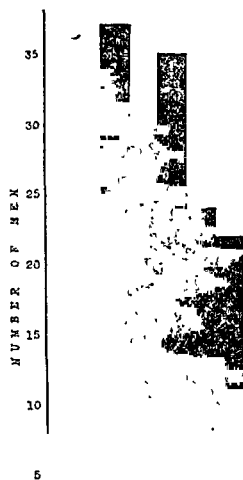
HOSPITAL DAYS OF CASES OF INADEQUACY

The 182 discharged men spent a total of 7405 days in the Station Hospital, for an average of 40.7 days per man. Their hospital admissions totaled 309 (Table 1). In the same period for

TABLE 1. *Hospital Admissions.*

No. of Admissions per Man	No. of Men	Total Admissions
One	90	90
Two	60	120
Three	19	57
Four	5	20
Five	2	10
Totals	182	309

the entire camp a total of 286,592 hospital days were required for all pathologic conditions encountered; these included an epidemic of influenza and an epidemic of measles. Thus, 2.6

FIGURE 1. *Duration of Service Prior to Discharge.*

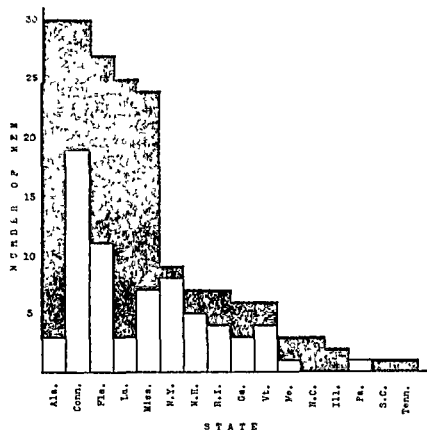
per cent of the total number of hospital days were utilized by the group of 182 cases under discussion.

It must be pointed out that only 16 of the 309 diagnoses with which these men entered the hospital carried any note regarding mental observation. In all other cases the men were ad-

mitted for organic complaints. Much of the time lost was on wards where such complaints were investigated and ruled out. The neuro-psychiatrist was called in only as a last resort.

TIME REQUIRED FOR RECOGNITION OF CONDITION

The period of time from induction until the condition leading to discharge was finally diagnosed varied from five days to eleven months (Fig. 1). It will be noticed that only 10 of the 182 men lasted in the service longer than six months, and that the peak for recognition

FIGURE 2. *Geographical Distribution by States.*

The unshaded blocks represent men from urban areas; the shaded ones, men from rural areas.

of the discharge condition was three months. This is probably a longer time than will be needed for recognition in the future. In the formative period of the camp, inept and unadaptable men were not subject to the same strain and surveillance as they will undergo henceforth.

GEOGRAPHIC DISTRIBUTION OF DISCHARGED MEN

The discharged men were classified by Army divisions, by states of origin and by their previous environments, rural or urban. The Dixie Division contributed 112 (0.62 per cent) of its total manpower of 17,942 soldiers, the New England Division 53 (0.32 per cent) of its 16,483 soldiers, and other units 17 men. These figures do not seem to reflect any differences in the caliber of the men from various parts of the country. A probable contributing factor was the fact that New England induction boards were somewhat more

efficient in weeding out subnormal material than those in other sections.

On the basis of figures given in the 1941 *World Almanac*, we listed all residents of towns of 2500 population or over as urban, and divided the discharges accordingly into rural and urban. We found that 70 (38 per cent) came from urban

engineers, and 12 were from the hospital medical detachment. Exact percentages cannot be given, but it is certain that the smallest incidence occurred in the infantry, the next in the artillery, the next in the engineering corps, and the highest in the hospital detachment. This indicates that the more technical the work required, the greater the

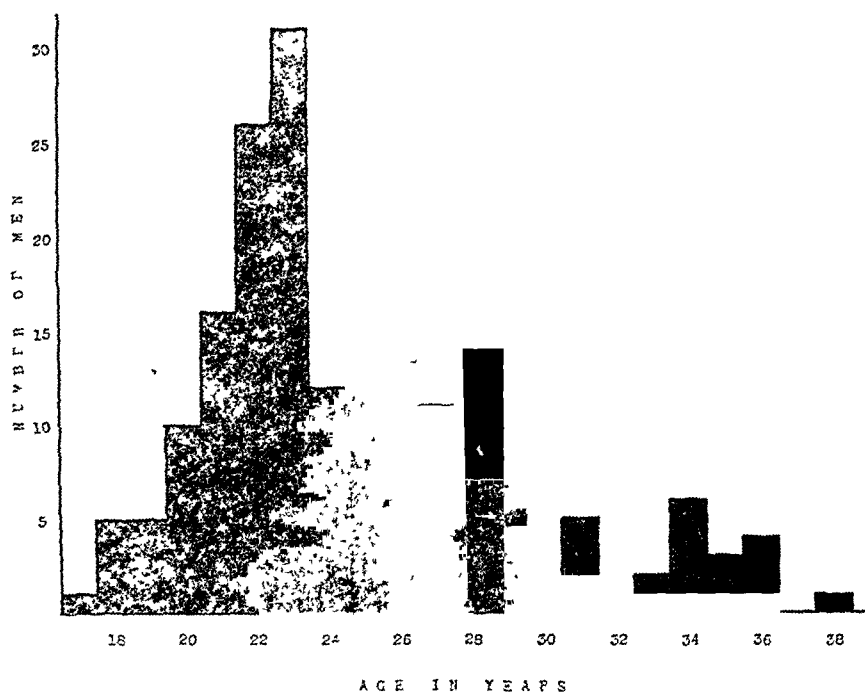


FIGURE 3. Age at Discharge.

communities and 112 (61 per cent) from rural communities. Figure 2 shows the preponderance of rural cases from the South. This is attributable to the predominance of farming as an occupation in that area. In a random sample of 3000 soldiers, 68 per cent came from rural and 32 per cent from urban areas. Therefore, much to our surprise, more city men proportionately were found inept or otherwise inadequate for military duty. This finding is diametrically opposed to the one we described in an earlier paper.³

AGE DISTRIBUTION

The age distribution of the men discharged (Fig. 3) was roughly parallel to that of the camp personnel as a whole. It demonstrates that inaptitude affects the same percentage of each group and that experience and increasing age do not enable the men to outgrow their difficulties. When the most frequent diagnoses, constitutional psychopathic state and mental deficiency, are considered this statement does not seem brash.

DISTRIBUTION BY TYPE OF MILITARY SERVICE

Of the 182 men discharged, 121 were infantrymen, 41 were from the field artillery, 8 were en-

likelihood that inaptitude will be revealed. The large number from the hospital detachment is especially significant. Possibly working in the hospital educated these men in the ways and means of successfully simulating the constitutional psychopathic state. The incidence in this group was several hundred per cent higher than that to be expected in the other types of military service. This suggests that henceforth an additional check should be placed on those in similar positions.

DISTRIBUTION BY RANK

The distribution by rank (Table 2) was as follows: 170 men were privates, only 6 were noncom-

TABLE 2. Distribution by Rank.

RANK	NO OF MEN DISCHARGED	PERCENT- AGE DIS- CHARGED	PERCENTAGE OF RANK IN THE ARMY
Private	170	93	52
Private, first class . .	6	3	30
Corporal	2	1	10
Sergeant	4	2	8
Total	182		

missioned officers, and only 6 were first-class privates. The extremely low proportion of first-class

privates, corporals and sergeants to privates, in comparison with the ratio in the Army as a whole of one noncommissioned officer to every four privates, shows that most company commanders made promotions wisely.

DISTRIBUTION BY OCCUPATION

Classification by occupation previous to military service (Table 3) was arbitrary. Each case was

TABLE 3 *Distribution by Occupation*

TYPE OF OCCUPATION	NO. OF MEN DISCHARGED	PERCENT ALL DISCHARGED	PERCENT IN THE ARMY*
Unskilled	105	58	28.7
Semi skilled	32	18	23.1
Skilled	19	10	20.2
Business	12	7	18.4
Professional	4	2	9.6
Never employed	10	5	0

*Based on 3000 soldiers

considered on its merits and given the full benefit of doubt; that is a higher rating was given whenever the question arose. Thus, store clerks were listed under "business," and truck drivers as "semi-skilled labor"; of the 4 men listed as "professional," two were students (exact status unknown), one was a Salvation Army fieldworker, and the last was a chiropractor. We admit that our generosity in rating is open to question; yet the occupational status of the series runs quite in accord with the expectation, the greater number of men being in the lower socioeconomic groups prior to induction.

DIAGNOSES

Mental deficiency was the reason for discharge in 67 cases. The Kent E G Y test was used as a standard and was supplemented by other tests whenever indicated. The mental ages are shown in Table 4. Almost all these cases were said

TABLE 4 *Mental Ages of Men Discharged for Mental Deficiency*

MENTAL AGE	NO OF MEN
Five years	1
Six years	2
Seven years	2
Eight years	15
Nine years	16
Ten years	19
Eleven years	8
Twelve years	4
Total	67

to show the "hypochondriasis of oligophrenia." Each presented multiple organic syndromes that required intensive investigation. Only when these had been disproved in the gastrointestinal, cardiac, urologic or other wards and much valuable time

had thus been spent did they finally reach the neuropsychiatric section.

Two men were discharged with a diagnosis of neurasthenia, gastrica. These diagnoses were probably erroneous, since it has been suggested by the Surgeon General's Office that such cases should receive a diagnosis of psychoneurosis, conversion hysteria. However, since these men were discharged under Section VIII they have been included in our series.

The rest of the men were discharged with a diagnosis of constitutional psychopathic state. This condition is classified by the *Standard Diagnostic Book* of the United States of America in seven groups: inadequate, paranoid, emotionally unstable, criminalistic, pathological liars, sexual psychopathy and unqualified. Of these, only three were used as the primary diagnosis: 55 men were listed as inadequate, 48 as emotionally unstable, and 19 as criminalistic. Occasionally, they were employed as secondary diagnoses.

In every case short but reasonably adequate histories were taken. So far as possible, childhood impressions, school records, former occupational situations, court and criminal records, sexual histories and personal relationships were probed

RECOMMENDATIONS

We believe that each selectee and enlisted man, prior to his final induction into the Army, should be placed in a replacement center for a probationary period of three months. During this time a competent psychiatrist should assist the company commander in weeding out those psychically unfit for military duty before marked breakdowns occur or severe inadequacies make themselves apparent. The great majority of these cases, as well as most undetected psychoneurotic patients, could thus be eliminated without ever being actually inducted. This would save the Army the expense of many hospital days and spare the selectees the mortification of complete realization of failure.

Furthermore, this trial period should be served without prejudice to the Government, and barring physical disability incurred during it, the enlisted man or selectee should have no claim against the Veterans' Bureau. This arrangement would make possible the saving of both time and money. It would also aid materially in eliminating future compensation claims. It is impossible to estimate how many constitutionally psychopathic persons and mental defectives are now collecting government pensions because of a few months spent in an Army training camp in the last war. Judging from our experience, they spent even these few months in the hospital—their sole contribution then, as it is now—only to hinder the war effort.

SUMMARY

A report is given of 182 soldiers discharged from the Army through the Station Hospital at Camp Blanding, Florida, under Army regulations providing for the release of men who are incompetent or inept, or have habit or personality traits undesirable in a soldier.

The number of hospital days used, the time required for the recognition of inadequacy, and the distribution by geographical considerations, age,

type of service, rank, civilian occupation and discharge diagnoses are discussed.

Some recommendations are offered to aid in the diminution of the number of these cases.

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MEDICAL PROGRESS

GYNECOLOGY: NEOPLASMS OF THE OVARY

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BOSTON

A REVIEW of the literature concerning ovarian growths shows that a large amount of information that is not generally possessed is now available. From the confusion of great numbers of ovarian cysts, cancers and benign tumors, considerable advance has been made in simplifying classifications and placing the various lesions in their proper niches. Robert Meyer¹⁻³ and Walter Schiller⁴ have especially been in the vanguard for separating the special types from the enormous heterogeneous group of a few years ago. Many growths once considered malignant are now considered benign, and many tumors of more or less definite histology have been shown to be functioning tumors. Americans who have made special contributions to the subject of ovarian cancer and its treatment and prognosis include Lynch,⁵ Geist,⁶⁻¹⁰ Frank,¹¹⁻¹² Taylor and Greeley¹³ and Pemberton.¹⁴ In this review it will not be possible to give credit to each investigator, but many important references are appended.

In a review of the literature it is perhaps not correct to present a classification of ovarian neoplasms, but the classification given below, based on Schiller's¹⁵ recommendations, seems to simplify the whole problem.

CLASSIFICATION OF OVARIAN NEOPLASMS

It is obvious that the ovary must contain in itself many potential growth cells. It commences as a clump of mesenchymal cells on the posterior wall of the abdominal cavity behind the forming peri-

toneum. This primitive group of cells furnishes those that under certain circumstances become specialized cells, some of which may eventually be indistinguishable from epithelial cells. For instance, the primitive connective-tissue cells of the early gonad may surround an ovum and become granulosa cells or theca-interna or theca-externa cells. In contact with spermatozoa these same cells may differentiate into Sertoli cells or the supporting cells of the testicular tubule. Sometimes the cells that usually become differentiated do not change toward male or female cells, but remain neuter and develop into the cells of the dysgerminoma or neuter tumor. The undifferentiated connective-tissue cells from which the differentiating cells arise form the stroma of the ovary, and from them may arise the fibroma and sarcoma of the ovary.

The epithelial covering of the ovary, arising as it does from the celomic epithelium of the pelvis, may differentiate into epithelial-like structures similar to those that arise from the celomic epithelium. As the celomic epithelium is the precursor of the müllerian ducts, it is easy to appreciate that epithelium similar to whatever the müllerian ducts might form may be present in the ovary. The upper vagina, the cervix, the endocervix and the endosalpinx are derived from these ducts. Therefore it is possible that squamous epithelium, endocervical epithelium, endometrial epithelium and endosalpingial epithelium may be present in certain tumors of the ovary. Schiller¹⁵ has demonstrated that the pseudomucin noted in the so-called "pseudomucinous cysts" of the ovary is not pseudomucin but old changed mucin. Thus, if pseudomucin is mucin in certain mucinous cysts, it is probably

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual*, Vol. III, 1942 (Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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derived from the cervical epithelium, such lesions being endocervical epithelial tumors. Simple cystadenomas, papillary cystadenomas, malignant papillary cystadenomas and solid cancers of all the above types therefore arise from the epithelium of the covering of the ovary. There is of course an unclassified group that may arise from a more primitive type of celomic cell.

Inasmuch as the primitive ovary grows in close proximity to the adrenal gland, the kidney and the primitive mesonephros and wolffian ducts, it is not surprising that tumors of these types are occasionally found in the fully formed ovary. Cells of organs arising near the ovary are incorporated in it during its growth and develop early or later in life. Thus the origin of the adrenal cell tumor of the ovary and the mesonephroma and Brenner tumor is explained.

The ovary contains ova, and if one of these should be fertilized, either parthogenetically or otherwise, the ovary would probably contain tumors or cysts of cells from all other organs or tissues of the body. These growths when solid and made up of undifferentiated or differentiated cells are called teratomas, whereas the cystic types as a rule contain all three germ layers and are known as dermoid cysts. Thus the fertilization of an ovum in an ovary may produce tumors similar to the thyroid gland, cartilage, bone, the central nervous system, the intestinal tract or any part of the epithelial system. A tumor of intestinal epithelium in a dermoid cyst can easily explain certain other of the so-called "pseudomucinous tumors," which are really mucinous tumors. Pseudomucinous peritonitis arises from these tumors, but in both men and women it may be present in patients with mucocoeles of the appendix. It is probable that the origin of such peritonitis is the mucus cells of the intestinal tract.

The ovary is also the seat of metastatic lesions. Tumors of the stomach metastasize to the ovary and are responsible for Krukenberg tumors, which are myxomatous in type and contain signet ring cells that secrete mucus. Endometrial cancers of the uterus metastasize to the ovary, and these tumors cannot be differentiated from malignant epithelial tumors of the ovary formed from the primitive endometrial cells of the celomic epithelium. Thus there are two types of endometrial cancers of the ovary, one formed from the covering of the ovary and one metastasizing to it from the uterus. Other organs of the body may be responsible for metastatic tumors in the ovary—small intestine, bile duct, breast, large intestine, rectum and even the pigment cells of the eye.

Thus it is clear that neoplasms of the ovary may be grouped into those arising from the celomic epithelium covering the ovary, from the

primitive mesenchymal cells, because of continuity and from fertilized ova and those metastasizing to it. The classification is as follows:

- Tumors arising from celomic epithelium (vaginal, endocervical, endometrial, endosalpingial)
 - Cystoma (endometrioma, endosalpingioma, adenoma, fibroidenoma)
 - Papillary cystadenoma
 - Malignant papillary cystadenoma
 - Solid carcinoma
- Tumors arising from primitive mesenchyme
 - Arrhenoblastoma
 - Granulosa cell, thecal cell
 - Luteoma, xanthofibroma theca cellulare
 - Disgerminoma (neuter)
 - Fibroma
 - Sarcoma
- Tumors arising because of continuity
 - Adrenal cell
 - Kidney cell (hypernephroma)
 - Mesonephroma
 - Brenner (renal pelvis, ureter or urethra)
- Tumors arising from fertilized ova
 - Teratoma, chorionepithelioma, struma
 - Dermoid cyst
- Metastatic tumors
 - From uterus (endometrial)
 - From stomach (Krukenberg)
 - From intestine (small or large), eye, rectum, breast, bile duct and so forth

These five sources include all the possible ovarian neoplasms, and such a grouping is not difficult to understand or remember. Physiologic cysts have been deliberately omitted because they are not true neoplasms but represent abortive ovarian function. Such cysts include atretic follicles, follicle cysts, corpus luteum cysts and thecal lutein cysts. These small cysts are important but should be considered in the abnormal physiology of the ovary and not among its neoplastic possibilities.

GENERAL CONSIDERATIONS

Careful and thorough investigations must be carried out in patients with ovarian tumors. Such investigations are those conducted in patients with abnormal bleeding, thyrotoxicosis, hirsutism, virilism, fluid in the abdomen and chest and increase or decrease in size of the breasts. One must be familiar with the technic of endometrial biopsy and peritoneoscopy. Laboratories must be available to determine the levels of follicle stimulating hormone, estrin and pregnandiol, to measure the basal metabolic rate, to perform Aschheim-Zondek and Friedman tests and to determine the excretion of the androgens and 17 ketosteroids—the latter being a representation of adrenocortical function.

It must be remembered that at operation a pathologist should be present who can help to de-

termine the type of tumor with which one is dealing. It is essential in modern surgery to be able to distinguish benign from malignant tumors. Tumors that appear malignant in gross may be relatively benign; such is the dysgerminoma, whose diagnosis is made more easily from a frozen section than from a fixed section. One should also be able to make a prognosis, based on the type of tumor found. Another reason for making a histologic diagnosis before the patient's abdomen is closed is to be certain that the tumor is not one that is likely to be bilateral, or to be of such a type that might metastasize to the uterine body and thence to the cervix. It is recognized that an occasional tumor will respond well to x-ray therapy: every gynecologist has had some patient who had metastases to the omentum or to the peritoneum, with fluid in the abdomen, and who, after removal of a certain amount of the primary tumor, responded to x-ray treatment, but these cases are rare.

The new syndrome^{16, 17} of abdominal and chest fluid due to fibroma of the ovary must not be forgotten; if a patient has a tumor in the pelvis with fluid in the chest and abdomen, one must not conclude at once that the lesion is malignant. It has been shown that the removal of a simple fibroma of the ovary may cure such a condition. It is also true that cystadenomas and malignant papillary cystadenomas of the ovary may be accompanied by pleural as well as abdominal fluid. Reports have been made by MacFee¹⁸ and Dannreuther¹⁹ of such fluid in benign lesions, and by Schenck and Eis²⁰ in a malignant one. Recently a similar case was seen at the Pondville Hospital; the patient, who had a cancer of the ovary with fluid in the chest, was probably cured by removal of the ovarian tumor — there were no malignant cells in the centrifuged chest fluid.

Today, adequate knowledge demands that the surgeon recognizes the type of lesion, if possible, that he knows the proper investigative laboratory technics, and that he realizes how and when to use x-ray treatment. The last has never cured patients, but it has helped to make them live longer. It must be outlined by the roentgenologist in such a way that it is directed toward the tumor, toward the spilled portions of the tumor or toward the adhesions connected with the tumor. It is of no use for the surgeon to write a note to the x-ray department saying simply: "Carcinoma of the ovary. Please treat." This practice should be abandoned.

TUMORS ARISING FROM CELOMIC EPITHELIUM

Cystomas of the ovary are true neoplasms and arise, as postulated, from the epithelium covering the ovary. They may be small or large; they may be single or multilocular; and they may contain serous or so-called pseudomucinous fluid.

The epithelium may be of the tubal, endometrial or endosalpingial type, or even of an unclassified type. The possibility that this lesion is bilateral is great; therefore both ovaries should be examined carefully. This lesion is not malignant, and its simple removal from the ovary, if possible, or removal of the ovary itself with a careful inspection of the other ovary, is all that is necessary, but the patient must be watched.

Papillary cystadenomas present a different problem. These are potentially malignant. If the papillary growths are all on the inside of the ovary and if they are filmy and small and not infiltrating, the chances of their being benign are very great. However, they may be malignant microscopically. They are bilateral in 30 to 40 per cent of cases. One finds in these lesions the type of epithelium that grows from Müllerian epithelium — squamous epithelial, endocervical or mucinous, endometrial or endosalpingial. Proper treatment for the papillary cystadenoma is removal of both ovaries. However, because many of these occur in young women in whom the preservation of fertility is essential, one can be conservative but must watch carefully to make sure that there is no occurrence in the other ovary, which may be of the malignant type. If the pathologist finds an area that is suggestive of cancer, the responsibility of the surgeon is great. Should he reoperate and take out the other ovary? No one can solve this problem but the surgeon himself. Should he elect to reoperate and remove the other ovary, no one could criticize him.

A *malignant papillary cystadenoma* demands close scrutiny. If a papillary cyst of the ovary shows thickness of the wall, penetration through the wall of the cyst to the other side or papillary areas on the outside of the cyst, one must be very suspicious of malignancy. The pathologist cannot always assure the surgeon, but if the tumor is considered probably malignant, radical surgery should be carried out. By radical surgery is meant the removal of the uterus and the cervix, because the presence of metastases in the uterine wall means that there may be metastases in the cervix. The opposite ovary is involved in a large percentage of cases; therefore it also should be removed. The prognosis for these patients is about 21 per cent survival for five years — a very small percentage of curability. It must also be remembered that metastases from endometrial cancer are very similar to the endometrial type of malignant papillary cystadenoma. One must determine by curettage of the endometrium whether or not it is involved primarily and the ovary secondarily, or vice versa. Most surgeons believe that x-ray treatment is unnecessary if the lesion is removed in toto without spilling or with-

out evidence of adhesions. If spilling has occurred or if there are evidences of adhesions and of growth onto the bowel or peritoneum, x-ray treatment must be given; and, if so, the case must be discussed with the roentgenologist so that the x-rays can be directed in the proper direction.

Solid carcinoma of the ovary is the most serious of all the epithelial growths of this organ. The curability is very low, 9 per cent survival for five years. It is believed, however, that if the patient lives for two and a half years following removal of such a tumor, the chances of permanent cure are very great.²¹ Patients with malignant papillary cystadenoma succumb more slowly than do those with solid cancers; if the solid cancers are cured, they are usually thoroughly cured. These tumors may be made up of the squamous-cell type of epithelium, representing the vagina, the mucinous, representing the endocervix, the endometrial, representing the endometrium, or the endosalpingial, representing the inside of the tubes; or they may be of an entirely unclassified type. Abnormal bleeding is not uncommon in these lesions. It is the general belief that the peritoneoscope is of great value in diagnosing this tumor, and it should be used frequently and without hesitation to determine whether the tumor can safely be removed or whether there are metastases throughout the abdomen. In spite of the fact that the abdomen and even the liver, or at least the surface of it, may be thus involved, one must consider removing the local growth, because for some reason or other this procedure may prevent rapid growth of these extensions. Metastatic areas and fluid have been known to vanish after removal of the primary growth; why, is not known. The question of dissecting lymph nodes in patients with solid cancer of the ovary is an important one. As yet this dissection cannot be advocated, but the time may come when, if more is known about where these metastases are likely to occur, removal of them will become part of the surgical approach. X-ray treatment should be given, as in malignant papillary cystadenoma, only when it is known where the tumor has extended.

Included in this group of celomic epithelial growths are the *endometriomas* and *endosalpingiomas* of the ovary and tube. These are benign lesions growing from the epithelium of the cortex down into the body of the ovary, forming the so-called "chocolate cysts." There is a difference of opinion whether these lesions come from the endometrium itself, the cells flowing through the tubes and alighting upon the ovary at the time of menstruation, or arise from the endosalpinx, attaching themselves to the ovary, or arise from the celomic epithelium covering the ovary. It is not unlikely that the last-named source is the primary one.

These cysts grow to moderate size before they are so pressed on by connective tissue and ovarian capsule that function ceases. There is no question that the endometrioma menstruates, but how long it continues to do so is doubtful. Endometriosis of the pelvis, which may arise from an endometrioma of the ovary that has become adherent to the broad ligament or to the cul-de-sac, may be a serious lesion demanding radical surgery. However, most gynecologists believe that if one can be conservative one should excise the endometrioma from the ovaries or ligaments and save the pelvic organs so that future childbearing can take place. It is also believed that pelvic endometriosis is increasing, perhaps because of avoidance or postponement of pregnancy. Normal childbearing is most important in order to prevent the onset or growth of this lesion.²²

TUMORS ARISING FROM PRIMITIVE MESENCHYME

The *arrhenoblastoma* is male-directed and is often, although not always, accompanied by virilism, masculinization, hirsutism and so forth. The testicular tubular adenoma of Pick is the most highly differentiated type. In patients showing physiologic effect of such a tumor the clitoris is enlarged, the scalp hair recedes, and the growth of hair increases in areas similar to those found in men; the breasts atrophy, the voice becomes deeper, and the patient assumes a mannish physique. Sometimes amenorrhea accompanies this tumor, but not always. The tumor may be small or large. It is usually freely movable and is not always malignant. It has been stated that removal causes the hair to recede, but it has been the experience of the Ovarian Dysfunction Clinic at the Massachusetts General Hospital that the hair does not recede but grows softer, without further increase. The voice rarely returns to normal, because there is an anatomic change in the larynx owing to the presence of this male tumor. The clitoris does decrease in size.

The diagnosis of this lesion in those in the menstruating age is not difficult because it so frequently causes amenorrhea and the above changes in the appearance of the patient. The follicle-stimulating hormone in the urine of such patients is extremely low, and the presence of a low titer of follicle-stimulating hormone, amenorrhea, hirsutism and the presence of an ovarian tumor indicate the diagnosis. Albright²³ thinks that a low titer of follicle-stimulating hormone is of extreme importance. The amount of 17-ketosteroids in the urine, which is primarily a measure of adrenocortical male hormone, is not necessarily disturbed; it may be high but usually is not. The arrhenoblastoma as a cause of symptoms should

The granulosa-cell tumor should be grouped together with the thecal-cell tumor from primitive connective-tissue directed toward the female after very early growths, as stated, and distinguishable from early antral follicles. Granulosa-cell tumors grow in undifferentiated or differentiated form. In some tendencies of attempts at follicle formation may be thought to be present, but usually proved to be areas of degeneration, the so-called "Call-Exner bodies." No corpora are present in granulosa-cell tumors. Kuder and Cadden²⁷ suggest that these tumors arise in the granulosa cells of follicles, as Fawcett²⁸ showed, arising in x-ray treated

[illegible]

cellulare or luteinized thecoma. These tumors are rare and are usually benign. They produce definite changes in the endometrium, causing a persistent secretory phase, and are often accompanied by marked decidual formation. Amenorrhea may be present. The presence of persistent secretory endometrium and periods of amenorrhea and bleeding when an ovarian tumor is present usually clinch the diagnosis.

The *disgerminoma* was formerly called a seminoma, as was the testicular tumor of the same histologic structure, but Meyer³¹ showed that this tumor does not arise from the seminiferous tubules of the testicle, but rather has invaded them; therefore the old nomenclature had an incorrect basis and he called the growth "disgerminoma." *Dis* means "both"¹⁵; that is, the same type of neoplasm occurs in the male and the female. In the male it is considered extremely malignant, whereas in the female it is frequently benign. Seegar³² says that the disgerminoma has a mortality of 35 to 60 per cent, basing his conclusion on 50 cases from the literature and on the results of treatment in 17 of 19 cases in his report. Of the 12 cases seen at the Massachusetts General Hospital, only 1 has proved to be malignant, and in that case the tumor had already begun to invade the surrounding tissue.

The disgerminoma is neuter; it arises from those primitive cells that might have developed into either granulosa or Sertoli cells but did not. It has no endocrine function. A large number of cases have been reported. The lesion can be recognized on frozen section as easily as from a fixed section. The tumor is made up of large round cells divided by connective-tissue-cell septa full of lymphocytes, and the presence of foreign-body giant cells is common. Disgerminomas were formerly called large round-cell carcinomas of the ovary; they were given x-ray treatment, and were frequently cured. The tumor is very radio-sensitive, but it is also benign in the majority of cases, and therefore x-ray treatment should not be given, because some of the young patients might otherwise be able to have children. Many times the patient herself is a neutral, that is, her genital tract is not normally developed. In many of the cases at the Massachusetts General Hospital, however, there was normal female development. Moehlig³³ reports a case of intersexuality in a patient with malignant teratoma of the seminoma type. He was probably describing a disgerminoma, and possibly one that arose in an ovario-testis. Long et al.³⁴ report a disgerminoma in a pseudohermaphrodite. Among the cases at the Massachusetts General Hospital was that of a young girl of seven, with pubic hair, open vagina and a large clitoris. Pregnancy occurred in 3 pa-

tients following removal of the tumor. These tumors are supposed to be common in the ovario-testis. The ovario-testis itself is a rare lesion, not being a tumor but a physiologic abnormality, the gonads being made up of both ovary and testis.

Fibromas of the ovary arise from the non-differentiating mesenchyme that is to become the stroma of the ovary. They are not uncommon. The size of the tumor varies from that of a small pea to that of an adult's head. It may grow on the outside of the ovary in papillary fashion or may include the whole ovary. Usually there is a firm capsule, and on section the tumor shows whirling areas of connective tissue as in uterine leiomyoma. It is well known that the condition is often accompanied by abdominal fluid. Recently Meigs and Cass³⁵ presented a number of patients with fibroma of the ovary with fluid in the chest as well as in the abdomen. Up to the present time 27 cases with fluid in the abdomen and chest have been reported in the literature.¹⁶ The fluid may be in the right or left chest, or in both. The reason for its occurrence is unknown. Probably the fluid is formed in the abdomen and enters the chest cavity by way of the diaphragmatic lymphatics. This entity is important because patients who have an ovarian tumor with fluid in the chest and abdomen do not necessarily have a tumor that is malignant and has metastasized to the chest. Chest taps with centrifuging of the fluid and examination of the cells is extremely important, because if no malignant cells are present one may be dealing with a fibroma of the ovary, and its removal will stop formation of fluid in the chest as well as in the abdomen. Reports are already appearing in the literature of patients who were given up as hopeless but were relieved by surgical removal of the benign lesion. Ovarian cysts have been reported with the same findings, as have leiomyomas of the uterus. It must be remembered that ascites alone can occur with any large benign pelvic tumor.

Sarcoma of the ovary is rare and arises from the same primitive undifferentiated cells that form the stroma. Patients with true sarcoma do not do well and the prognosis is poor. If the diagnosis is made, removal of both ovaries is best. Removal of the uterus is not essential in these cases, since it is rare for metastases to occur there. Reclassification of sarcomas of the ovary in the laboratory has in many cases proved them to be other types of tumors.

TUMORS ARISING BECAUSE OF CONTINUITY

The *adrenocortical-cell* tumor is among the group arising from continuity. Inasmuch as this part of the adrenal gland contains a male-directed hormone, such a tumor in the ovary may produce

masculinization, hirsutism and so forth, just as may an adrenocortical cancer, tumor of hyperplasia. Novak³⁶ has recently reported 3 patients with adrenal-cell tumors of the ovary with masculinization. Clear-cell tumors of the ovary, so often considered as adrenal, are not necessarily of the masculinizing type, nor are they necessarily adrenal. They may be clear-cell carcinoma of the kidney, the *hypernephroma*. This tumor is not accompanied by any definite symptoms. Van Kirk and Edwards³⁷ describe a hypernephroma of the ovary. A patient with a functioning adrenal-cell tumor of the ovary may become masculinized with male configuration, hair, large clitoris, change in voice, amenorrhea and so forth. There may or may not be a change in the sugar metabolism, but one would certainly expect it. There should be an increase in the excretion of 17-ketosteroids. The presence of an ovarian tumor accompanied by the above symptoms should be investigated by all available laboratory methods, and differentiation from an arrhenoblastoma is difficult unless the 17-ketosteroids and the sugar curve are estimated. If the 17-ketosteroids and sugar metabolism are upset, the adrenal glands should be explored by air injection and an intravenous pyelogram. If nothing abnormal is found, surgery should be undertaken, and there are definite possibilities of finding an active adrenal tumor.

The *mesonephroma*, which Schiller³⁸ has described, contains primitive glomeruli and probably arises from the primitive kidney or mesonephros. It occurs in the ovary because of the closeness of the mesonephros to the primitive gonad. These tumors are probably benign, and conservative treatment is usually the method of choice; however, Rosenblatt and Grayzel³⁹ have recently recorded a malignant mesonephroma.

Tumors of the *Brenner* type probably arise from the type of epithelium that is present in the kidney pelvis, ureter and urethral orifice.⁴⁰ Small clumps of stratified transitional epithelium are found in areas in the ovary, which has the appearance of a fibroma. Novak and Jones⁴¹ believe that Brenner tumors arise in the Walthard islands of indifferent cells in the ovary, and that the epithelium cells of the Brenner tumor may develop into pseudomucinous cells and later form pseudomucinous cysts. The Brenner tumor is found along with the so-called "pseudomucinous cystadenoma," and it is possible that this lesion might arise from a teratomatous development. The epithelium, however, is probably representative of the epithelium of the urinary tract.

TUMORS ARISING FROM FERTILIZED OVA

The fertilized ovum in the ovary may produce any sort of tumor or cyst. The ovum is considered as fertilized parthenogenetically, or the tera-

toma may be considered as a twin of the host. Fertilization occurs in some manner that we cannot explain. Shaw⁴² does not believe in the parthenogenetic theory but thinks that teratomas may arise from some functioning sex cell. He supports his belief by stating that most teratomas are formed of adult cells; if they were to arise from a fertilized ovum there should be a trophoblast, but there is none. He concludes that he does not know the origin of these tumors.

The *teratoma* is usually solid, composed of one type of tissue, such as thyroid, nerve tissue, cartilage and so forth, although Smeltzer⁴³ reports a solid malignant teratoma with three germ layers. The cells may be primitive and unrecognizable as being of any particular type, and in some cases are so undifferentiated as to be called embryonal. This represents the most primitive type of teratoma. Teratomas may or may not be malignant. They may invade and metastasize. If definitely malignant, radical surgery should be undertaken, with removal of the other ovary, the uterus and the cervix. If the malignancy is doubtful, radical surgery is still the best procedure.

Dermoid cysts are highly differentiated types of teratomas made up of two or three of the germ layers and often containing nerve tissue, skin, hair, teeth, bone, cartilage and so forth. Some of these lesions are malignant; most are benign. It is possible for a dermoid cyst to show malignant-looking areas and yet be a benign lesion. This picture is similar to what one sees in the parotid-gland mixed tumors, where there may be the most active-appearing carcinoma, and yet if any cartilage is found in the same tumor it is usually a locally malignant lesion only. Such a tumor will recur, but will not metastasize. Dermoid cysts with malignant areas act in the same way; that is, they may be malignant in appearance only, but they can be and sometimes are extremely malignant. The usual treatment of the simple dermoid cyst is excision with the ovary or excision from the ovary. About 8 per cent of these cysts are bilateral.

Chorionepithelioma of the ovary must be considered as a teratoma. Simard⁴⁴ has recently seen 2 cases of chorionepithelioma and believes in its parthenogenetic origin. Such a lesion would of course give a positive Aschheim-Zondek test, being composed of chorionic tissue. The chorionepithelioma is occasionally extremely malignant.

In the teratoma group there may be pseudomucinous cystadenomas arising from epithelium similar to the epithelium of the small intestine. Such a tumor is similar in appearance to the pseudomucinous cystadenoma of the endocervical type described above. The presence of hair or cartilage in such a cyst places it in the teratoma group.

Otken⁴⁵ has recently reported a primary mel-

anotic sarcoma of the ovary. This rare lesion is probably of teratomatous origin.

Struma or thyroid tumors of the ovary are not very rare and may include the whole tumor or a small area in a cystic growth. The thyroid tissue appears to be normal, and its iodine content is the same as that of normally placed thyroid tissue. Emge¹⁶ believes that 5 per cent of these tumors are toxic, and he reports a typical case. He quotes other authors with apparent authoritative cases. These tumors are usually benign but may be malignant.

METASTATIC TUMORS

The commonest metastatic tumor of the ovary is that due to the metastasis of *endometrial cancer*. There is often difficulty in recognizing whether this metastasis has occurred, or whether the endometrial type of cancer in the ovary is primary there, growing from the celomic epithelium. It is important, therefore, to curette patients with ovarian cancer in order to be sure that there is no cancer in the endometrial cavity. It has been the experience of most surgeons that involvement of the ovary from endometrial cancer indicates a very bad prognosis.

The *Krukenberg tumor* of the ovary, a metastatic tumor, is usually bilateral and smooth and has a thick capsule. On section it is myxomatous and suggests sarcoma. There is considerable controversy whether or not there is such a thing as a primary Krukenberg tumor of the ovary, there may be, but such a lesion should be considered a teratoma. Certainly the usual tumor is metastatic, the primary tumor being in the stomach. They arrive in the ovary by way of the retroperitoneal lymphatics and the lymphatics of the mesosalpinx, mesoovarium, uterine wall and tube, and are usually full of cancer cells. The gastric cancer cells do not float down to the pelvis, alight upon the ovary and then grow. This type of growth is not papillary on the outside of an ovary but is smooth and symmetrical and has obviously grown from the inside of the gonad.

Tumors of the small intestine metastasize to the ovary, and although similar in gross to Krukenberg tumors are frequently adenocarcinomas. Those metastasizing from the large bowel and rectum are of the same type as the primary ones; they are usually unilateral. In patients with widespread lesions of the breast or of the bile ducts, involvement of the ovary is not uncommon, but it is rare to find a tumor of the real Krukenberg type, that is, bilateral, large, smooth tumors. The metastasis of breast cancer to the ovary is usually a terminal finding. If, at operation, tumors of the ovary are found that are bilateral, smooth and kidney shaped, a primary source in the stomach

or intestine must be searched for. There are tumors from other sources that may metastasize to the ovary, such as melanoma of the eye, cancer of the cervix or tube and so forth.

SUMMARY

This discussion of ovarian tumors demonstrates that more tumors have been grouped together and that a simpler classification is possible. Many tumors of highly specialized types have been removed from the large group of ovarian tumors and more appropriately reclassified. Functioning or endocrine tumors have been recognized.

The treatment of certain ovarian lesions is definite and may be conservative, but the proper treatment of malignant ovarian epithelial growths is by means of radical surgery, with removal of both tubes, both ovaries, the uterus and the cervix. It is important to recognize that the other ovary should be removed in malignant papillary cystadenoma or solid cancer because of the large percentage of these tumors that are bilateral, and that the uterus and cervix should be removed because of the possibility of metastases into the uterus and thence into the cervix.

It has been demonstrated that x-ray treatment is not too successful and must never be allowed to influence the surgeon as against radical surgery. Roentgen ray treatment will prolong life but will not cure the patient. It has been obvious in all clinics that the x-ray treatment given in the past has not necessarily been given over the area of the extension of the growth. It is extremely important that the roentgenologist be shown by the surgeon where the tumor has been left behind or spilled so that the x-rays can be properly directed.

Knowledge of the pathology and histology of these tumors is of great importance. The presence of a pathologist at the operation is essential, for an expert can often differentiate one type from another. Thus the pathologist can help in the decision of whether or not to be radical.

If a mistake has been made and an ovary left in that might be involved, either because the tumor is often bilateral or because of the chances of a metastatic lesion, it is better to reoperate than to risk x-ray treatment. X-ray treatment should not be used to replace radical surgery.

Ovarian tumors are now receiving the attention of the endocrinologist and the medical man as well as the surgeon and the pathologist, which is well. The presence of functioning tumors of endocrine type has greatly increased the interest in all ovarian tumors. Special tests and special methods of investigation are now undertaken in patients who have abnormal physiologic responses possibly due to a tumor of the ovary.

means cancer. Tuberculosis, bronchiectasis and lung abscess may cause streaked sputum intermittently. A constantly bleeding process is usually due to a growing and friable tumor.

The complaint of chest pain favors cancer. Although an abscess with pleural inflammation gives pain, it is rarely so constant and severe as indicated here.

At this point, on the basis of history alone, I should make a presumptive diagnosis of cancer. What additional evidence must we examine?

The age of the patient favors cancer. His sex gives at least a four-to-one chance in favor of the diagnosis.

Physical examination only confirms what we suspect. The chest signs are consistent with an inflammatory process in the left lower lobe. The absence of a wheeze is not necessarily disturbing. A persistent wheeze always means a bronchial obstruction, but wheeze may be absent in varying degrees of blockage. Palpable axillary nodes in an elderly emaciated patient can be given no weight.

The laboratory was noncommittal. There was a mild degree of anemia, and a slight leukocytosis. Negative but weighty evidence is given by the sputum reports, on the basis of which I have excluded tuberculosis.

May we have the x-ray films?

DR. JAMES R. LINGLEY: Here is the cavity described lying in the middle of the left lung field. Its walls are thin and smooth, and there is a well-defined fluid level in its upper third. In the lateral view, the cavity is seen to lie posteriorly and to occupy the apex of the lower lobe. A Bucky film shows no evidence of rib or spine involvement, the bones appearing normal except for generalized decalcification. The lungs also show emphysema and an old tuberculous infection of the right upper lobe, which is probably healed. The left costophrenic angle is obliterated by a small amount of fluid or thickened pleura.

The heart is small, and the aorta shows marked tortuosity, with definite dilatation of its ascending and arch portions.

DR. DAVENPORT: The roentgenograms show only a large abscess. There is no demonstrable tumor mass or sign of bony metastasis. This evidence is equivocal, as neither is necessary to sustain a diagnosis of bronchial cancer.

Summing up the findings then, we have a sixty-five-year-old man complaining of cough, persistent chest pain and constantly streaked sputum, with a demonstrable abscess and a sputum negative for tubercle bacilli. My working diagnosis on these findings is bronchial cancer with secondary abscess.

What treatment are we justified in offering such a man? If we are correct, he is doomed to a progressive and painful course terminating in death. An exploratory operation is certainly justified. Suppose we are wrong, what weight should we give that possibility? The outlook for cure in an abscess of such size and duration is uniformly poor. Dr. Richard H. Sweet* has found no case of spontaneous cure in such abscesses with a duration greater than six months. Our patient is still faced with a slower, less painful, but progressive process, which untreated may eventually cause death.

Knowing the outlook with less bold measures in either case, I should accept the risks of exploratory operation. Further decisions must await the findings at the time of operation. Drainage would be palliative only. With an irreparably damaged lower lobe, its removal, whether for abscess or cancer, offers the only hope of permanent cure.

DR. EUGENE R. SULLIVAN: Dr. King, you saw this case. Would you care to comment?

DR. DONALD S. KING: I saw this patient in consultation, and I know what was found at operation, so that I can hardly approach the problem of diagnosis with an open mind. I do, however, wish to give hearty support to Dr. Davenport's insistence that bloody sputum over a long period almost always comes from carcinoma. This is particularly true if there is bloody mucus rather than blood mixed with pus. In retrospect the diagnosis in this case seems almost established by the persistent bloody expectoration, with obvious weight loss and chest pain.

When I first saw the patient I advised against bronchoscopy or operation and suggested a trial of chemotherapy. Former experience, however, had given us little hope that sulfadiazine would have a favorable effect on such a chronic abscess.

I wonder whether bronchoscopy would have given a diagnosis and whether it would have helped in the handling of the case. Dr. McGahey helped in the operation, and I should like to have his opinion whether the process was so located that it could have been seen through the bronchoscope.

DR. CLAUD E. MCGAHEY: I believe it was so located. However, I am against the routine use of bronchoscopy in persons of this age group.

DR. KING: I think that I advised against bronchoscopy for two reasons: first, because of the patient's general condition and, second, because of the lack of clinical or x-ray evidence of bronchial obstruction, either partial or complete. I do not, however, have a dread of bronchoscopy if prop-

*Sweet, R. H. Lung abscess: an analysis of the Massachusetts General Hospital cases from 1933 through 1937. *Surg., Gynec. & Obst.* 70:1011-1021, 1940.

erly performed, and I should like Dr Davenport's opinion concerning the risk in this case

DR DAVENPORT I should not favor bronchoscopy here. We have rarely found a cancer in the range of bronchoscopic biopsy where there has been no wheeze or x-ray evidence of obstruction. Secondly, as I see the situation, I am committed to an exploration with or without a preliminary biopsy, and the results of bronchoscopy would not change the plan of treatment. A factor in a borderline case is the slight but admitted risk of bronchoscopy in a man showing x-ray evidence of a dilated and probably eggshell brittle aorta. I should accept this risk if I felt bronchoscopy might give evidence that would dictate the plan of treatment.

CLINICAL DIAGNOSES

Abscess of lung
Bronchiogenic carcinoma?

DR DAVENPORT'S DIAGNOSES

Bronchiogenic carcinoma
Secondary abscess

ANATOMICAL DIAGNOSES

Epidermoid carcinoma (Grade II), bronchiogenic
Abscess of lung

PATHOLOGICAL DISCUSSION

DR SULLIVAN Dr McGahey, you participated in the operation. Will you tell us your findings?

DR MCGAHEY I had the opportunity to follow this case with Dr Churchill, who subsequently operated on the patient. Efforts to establish a definite diagnosis did not include bronchoscopy because we thought that the procedure was too risky in a man of this age with a dilated and rigid aorta.

We questioned the benefits to be gained from external drainage but concluded that if we could minimize the cough by such a procedure the patient might be made temporarily more comfortable. The operation was thus undertaken primarily with palliation in mind and secondarily to establish a diagnosis that, in the event of malignant disease, would justify x-ray therapy later.

The seventh intercostal space was exposed over the left paravertebral area. The intercostal muscles were found to be moderately edematous. Needle aspiration recovered a few cubic centimeters of moderately thick nonfoul pus from a point about 5 cm deep to the eighth rib. A segment of the eighth rib was resected, and the subjacent tissue was found to be firm and rubbery, and grated under the cut of the knife. A biopsy specimen was taken. The cavity was then opened through this tissue and found to contain about

40 cc of nonfoul pus. Tube drainage was established.

Convalescence was uneventful. The cough was considerably lessened, but when discharged the patient was still having moderate discomfort in the wound.

DR SULLIVAN Microscopic examination of the material removed at operation showed an epidermoid carcinoma of comparatively low grade malignancy. It is therefore evident that the abscess was secondary to the neoplasm, as Dr Davenport predicted.

DR KING Was lobectomy considered?

DR MCGAHEY The growth had extended through the pleura at the site of drainage. In any event this man would not have been a reasonable lobectomy risk.

CASE 29022

PRESENTATION OF CASE

A thirty-three year old housewife entered the hospital complaining of frequency, nocturia and incontinence of one year's duration.

The patient's husband had been injured in an automobile accident fourteen months previously, and since then she had been very nervous. One year before admission she developed urinary frequency and slight nocturia, and on several occasions during sleep she had total incontinence. Urinary incontinence was very frequent during any emotional disturbance. There was no dysuria, chills, fever or weight loss, but the patient had noted tremor, sweating and emotional instability. For the two weeks prior to entry she had had five or six bowel movements daily and also mild epigastric distress after meals. There were no menstrual abnormalities.

She had had thyroid enlargement for a number of years and had been treated until ten years before entry. She had had a mild "nervous diarrhea" for three months, five years previously. She had five children, all born at home, no perineal repair had been performed.

Physical examination revealed a well developed and well nourished woman with warm moist skin, moderate flushing and dermatographia. The eyes were normal. The thyroid gland was slightly enlarged. Examination of the heart and lungs was negative. The abdomen was flat and soft. In the right lower quadrant was a nontender movable mass measuring 4 by 1 cm. Pelvic examination showed a slight rectocele and cystocele and a little prolapse of the urethra. No incontinence was demonstrated. The cervix contained a few nabothian cysts. The fundus of the uterus was not enlarged and was in normal position.

Carcinoma can be fairly well excluded, chiefly on the basis of lack of mucosal involvement.

Lipomas and leiomyomas occur in this area in the wall of the cecum. They are both rare. I do

Acute appendicitis is so frequent that very atypical forms of it are as common as any of the rare lesions of this area. However, in the absence of any history of pain and tenderness, I cannot make



FIGURE 1. X-ray Films before (A) and after (B) Evacuation of a Barium Enema. The arrows point to the minimal swelling of the mucosa of the terminal ileum.

not ever hope to make a preoperative diagnosis of either.

Large lymph nodes about the ileocecal valve, as part of a lymphomatous process or tuberculosis, could give a palpable mass indenting the cecum. However, these diagnoses could be made only by inference from evidence of either disease elsewhere in the body.

Regional enteritis sometimes starts in this way and produces a similar mass. However, there are usually more gastrointestinal symptoms than are recorded, and some pain. Moreover, the mass is often tender, at least slightly. There are ordinarily some fever and weight loss. The x-ray films are interpreted as showing only a pressure defect on the cecum and spasm of the ileum without sign of ulceration. In the face of the foregoing evidence I cannot make a diagnosis of regional ileitis.

that diagnosis. Still I would not be greatly surprised if this were a subsiding acute appendicitis.

Mucocoele of the appendix should be considered. A true mucocoele of the appendix is rare. They are usually larger than this and likely to give more local symptoms. In some cases there exists an antecedent history of appendicitis. A certain number of cases are believed to follow a ruptured appendix, with subsequent resolution and formation of a cystic cavity containing mucus. Wangenstein* has produced mucocoeles in animals in this manner.

Finally, carcinoids are rare, but the appendix is by far the commonest site in the gastrointestinal tract for this tumor. They may be locally recurrent or metastasize to the regional lymph nodes. They give mild irritative or obstructive symptoms

*Wangensteen, O. H., and Dennis, C. Experimental proof of the obstructive origin of appendicitis in man. *Ann. Surg.* 101 629 647, 1939.

as they progress. They occur at practically any age but most commonly in the thirties.

Before concluding, there remains one more aspect to be explained. The patient is described as having emotional instability, tremor and sweating. I cannot readily explain these symptoms, and I do not know how definite they were. Perhaps she was just a nervous housewife. They could represent residual hyperthyroidism. There is mention of some kind of thyroid trouble ten years previously. But the essentially normal basal metabolic rate, the normal pulse and the lack of cardiac enlargement after all these years are against it.

One might conceive of a remote interrelation of the nervous symptoms, the hypertension and the right-lower-quadrant mass. Carcinoid tumors are argentaffinomas and developmentally related to adrenal medullary tumors, which have been described as causing paroxysmal hypertension. But carcinoids are nonfunctioning tumors, so far as I know.

In summary, I attribute the urinary symptoms to post-partum damage of the pelvic floor. The emotional symptomatology and tremor can be assigned to a psychic origin. In the absence of more gastrointestinal data and on the basis of a small nontender movable mass indenting the lower part of the cecum, I hazard the diagnosis of carcinoid of the appendix.

DR. EUGENE R. SULLIVAN: Dr. Bartlett, you saw this case. Will you add to the discussion?

DR. MARSHALL K. BARTLETT: As stated in the history and as emphasized by Dr. Sarris, this patient's presenting complaint was urinary incontinence. The story was much more definitely one of straight exertional incontinence than is given in the summary, and we were satisfied that it was explainable on the basis of the trauma of repeated childbirth.

The finding of a mass in the right lower quadrant was entirely incidental, but once it was found it was obvious that its nature must be investigated and explained before dealing with the chief complaint.

In evaluating this patient before operation, our line of reasoning followed much the same pattern as that outlined by Dr. Sarris. We excluded a tumor of pelvic origin on the basis of the physical examination, and ruled out an intrinsic lesion of the cecum or terminal ileum by virtue of the x-ray findings. Some process involving the appendix seemed the best explanation for the constant pressure defect of the cecum, and we believed that either a mucocele or a carcinoid would be found.

DR. SULLIVAN: Dr. McKittrick, will you tell us about the operative findings?

DR. MCKITTRICK. We operated on this patient thinking she had a tumor of the appendix, possibly a mucocele or a carcinoid. The barium enema had shown a pressure defect of the cecum (extrinsic), and the fluoroscopist was satisfied that the terminal ileum was normal. However, the terminal ileum proved to be the site of an early but well-established and typical regional enteritis. The bowel wall was uniformly thickened, slightly pale and less pliant than normal. The lacteals were prominent. Enlarged soft lymph nodes were scattered throughout the entire small-bowel mesentery. The process extended 25 or 30 cm. proximal to the ileocecal valve, gradually shading off to normal small intestine about 45 cm. from the cecum. The latter was a little thickened and injected. We were faced with the problem of what to do about this serious situation. The patient presented none of the usual requisites for surgery, namely, obstruction or fistulas. In fact she had been bothered by her disease only on two short occasions. Experience with early cases of regional ileitis has produced equivocal data regarding the benefits to be gained from early surgery. However, this seemed an ideal case to benefit from surgery if the adherents of early radical excision are correct. An end-to-side ileo-transverse colostomy was done as the first stage of a two-stage right colectomy. During the subsequent operation, all the grossly involved ileum and as much of the mesentery as could be obtained were removed. Still later, a urethroplasty was done to cure the urinary incontinence.

DR. GRANTLEY W. TAYLOR: What was done with the distal bowel?

DR. MCKITTRICK: The open end was turned in.

CLINICAL DIAGNOSES

Mucocele of appendix?

Carcinoid of appendix?

Urinary incontinence, due to urethrocele.

DR. SARRIS'S DIAGNOSES

Carcinoid of appendix.

Relaxed pelvic floor, with incontinence.

ANATOMICAL DIAGNOSES

Regional ileitis, acute, active.

Normal appendix.

PATHOLOGICAL DISCUSSION

DR. EUGENE R. SULLIVAN: The last 25 cm. of terminal ileum showed a thickened wall with an edematous mucosa. Just proximal to the ileocecal valve the edema was more marked and accom-

panied by a few shallow mucosal ulcerations. The largest of these measured 1.0 by 0.3 cm. The attached mesentery of the small bowel contained many soft lymph nodes. Microscopically these showed no resemblance to the picture seen in sarcoid. The appendix was completely normal.

DR. McKITTRICK: Would a small-bowel series have revealed a clue to the true diagnosis?

DR. LINGLEY: I doubt that further examination of the small bowel by a barium meal would have led to the correct diagnosis. On these films there is excellent retrograde filling of the terminal ileum, and I should say again, even in retrospect, that the mucosa appears normal.

DR. SARRIS: Do you now believe that the serrations represent ulcerations?

DR. LINGLEY: They undoubtedly do.

DR. ALFRED KRANES: I should like to ask Dr. McKittrick why he considered this to be an early case of regional ileitis. What about the history of diarrhea five years previously? We know very little concerning the natural history of this disease.

DR. McKITTRICK: I confess that I used the adjective "early" to signify not the duration of the disease but the degree to which the pathologic process had progressed. The disease may well have been present five years, but it had not yet appreciably narrowed the lumen of the bowel.

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THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

HALF A MILLION TYPEWRITERS

It is an interesting commentary on the magnitude of the enterprise in which we are currently engaged that the City of Magnificent Distances, wherein is lodged the very nerve center of our efforts, has issued an appeal for five hundred thousand used typewriters. It seems incredible that there should be so many key positions.

One of the inalienable rights of a democracy is that on going to war it should have two fronts—the aggressor nations, the professional fighters, avoid this until the last ditch, but we insist on having our real front and our paper front. The Battle of the Solomons has its quiet periods, but the Battle of the Bureaus never ceases.

There has been some sniping lately on the latter front, which seems to be one of bureaucracy

versus the business of the Nation,—and that business at the moment is war and war production,—and a few of the absurdities of how a bureau does its work have been pointed out. The story has been told, for instance, of the “tired businessman,” trying to consummate a contract with a departmental office in Washington, who was required to obtain fifty-one signatures for his papers. And a federal co-ordinator has been defined as one who brings organized chaos out of regimented confusion. Then, the *Reader's Digest* gives us the story of a subordinate in the War Department, enthusiastic and therefore probably young, who suggested the destruction of a large accumulation of tattered and obsolete records. The written proposal went up the line from one office to another until it, too, like a rolling snowball, had acquired a formidable bulk of its own. Approval after approval was attached to it until finally it reached the ultimate authority; permission was given to burn the papers—provided that copies were made of all those destroyed.

The *Journal of the American Medical Association* takes strong editorial notice in its November 7 issue of the report of Senator Pepper's Subcommittee on Manpower of the Senate Committee on Education and Labor. Apparently ignorant of the inventories of available medical personnel made by the American Medical Association in 1940 and by the Procurement and Assignment Service in 1941, the committee proposes the establishment of still another civilian authority to supervise and control the drafting and recruiting of physicians. So do republics stagger and fall under the burden of their own accumulated processes of government.

Typewriters, we know, are a necessary part of the equipment of our navy from dockyard to submarine; our military establishments need them from Ayer, Massachusetts, to Sydney, Australia; on our far-flung battle lines their keys, poked by the ponderous forefingers of countless staff sergeants, crackle above the staccato notes of the tommy guns; and that is where they should go. If they are wanted mainly in the Nation's capital,

however, and if, as has been suggested, the true purposes of democracy are being buried beneath a mass of protocols, then the need for half a million typewriters reveals, as Mr Churchill would say, the very belly of the monster

THE DOCTORS MAYO

A WAS a little man of English, Flemish and French Huguenot ancestry born in the neighborhood of Manchester, England, the son of a seaman, having pursued a medical education in Manchester, Glasgow and London without staying long enough to get a diploma, decided at the age of twenty five to try his fortunes in America. This was William Worrell Mayo. He was a pharmacist in Bellevue Hospital, New York, in 1845, he followed the westward trek to Buffalo, thence to Indiana where, in Lafayette, he opened a tailor shop, and then pursued medicine again and received a degree in 1850 from the Indiana Medical College at La Porte. "He was never satisfied with things as they were, but always wanted to go further," wrote his son later. Accordingly, with his Scottish American wife, he went on to St Louis, where he obtained a medical degree from the University of Missouri, and to St Paul, he explored the new settlements in the Lake Superior district, was attracted by the fertile valley of the Minnesota River, became pursuer on a river steam boat and publisher of a newspaper, manufactured patent medicines, and settled for a time and began the practice of medicine in Le Sueur, where, on June 29, 1861, was born a son, christened William James. He failed to get a commission in the Civil War, but was in the thick of the defense of the frontier settlements in the Sioux uprising and was foremost in the care of the wounded. Finally, in 1864, attracted by the boom town of the new wheat country, he moved to Rochester, where, on July 19, 1865, a second son, Charles Horace, was born.

Dr Mayo became the horse and buggy doctor of the district — active, enterprising and ambitious. He used a microscope, gathered a library, organ-

ized medical societies, went on study trips to New York and Philadelphia and returned to practice the new surgery. For the two sons, the life was that of country boys: school, chores, sport and, especially, helping their father with his work. "It never occurred to us that we could be anything but doctors." Will went to the newly founded medical school of the University of Michigan at Ann Arbor, where his career was not impressive six years later, in 1888, Charlie graduated from the Chicago Medical College (affiliated with Northwestern University), where he sat under Senn, Fenger, Andrews, Davis and Dudley — good teachers and, fortunately, converts to Listerism. Without the advantage of hospital internships the boys went back to Rochester to help their father. To young Dr Will is attributed the statement: "I expect to remain in Rochester and to become the greatest surgeon in the world."

The "old doctor," as he was then called, had become the most widely consulted surgeon of the region. He had operated on thirty six ovarian cysts, with a mortality of 25 per cent. He had not adopted Listerism.

Young Dr Will made trips to New York for postgraduate study, watched the work of Sands and Gerster, became convinced of the value of Listerism, and brought it back to Rochester. In 1883, a tornado swept the town, and the total lack of facilities for care of the wounded, who had to be placed in a dance hall, suggested to Mother Alfred of the Sisters of St Francis the need of a hospital, which was duly built (it is said against the advice of Dr Mayo). Thus was founded St Mary's Hospital, with the "old doctor" as consultant and the sons in active charge.

It is impossible to trace adequately the growth of the Mayo enterprise. At first, the brothers assisted each other without specialization, but gradually Dr Charlie took charge of diseases of the eye, ear, nose and throat, bones, joints, nervous system and thyroid gland, and Dr Will covered the abdomen, pelvis and genitourinary system. Sister Joseph succeeded Mother Alfred and, besides having general charge, acted for years as

Dr. Will's first assistant at operations. Dr. Stinchfield, a local practitioner, was associated in the medical field, and later Dr. Christopher Graham. The sick and injured of a wide and increasingly populous countryside, having no nearer consultants than the Twin Cities, flocked to Rochester. Associates were added to the staff whose names are almost as familiar as their chiefs': Plummer, Judd, Wilson, MacCarty—to mention but a few of the older group. Addition after addition was made to St. Mary's, laboratories were established, hotels erected and used in part as hospitals, specialties inaugurated, and new office facilities and ambulatory clinics provided. In 1912, a system of fellowships was devised through which young graduates—on moderate stipends—could observe, learn and provide services. In 1915, a million and a half dollars was appropriated from surplus earnings to create the Mayo Foundation for Medical Education and Research, as a graduate department of the University of Minnesota, and four years later all the assets of the Mayo Clinic were conveyed to a trust to provide for the perpetuation of the clinic. The last great physical expansion was the completion of the new clinic building in 1938 at a cost of three million dollars—a skyscraper of fifteen stories surmounted by a bell tower with a carillon. In that year, Dr. Will ceased operating, and a year and a half later, a retinal hemorrhage wrote finis to Dr. Charlie's surgical work.

There is no mystery in the success of the Doctors Mayo. "Stress the unusual opportunity that existed in the time, the place, the general setup, not to be duplicated now," said Dr. Will, in authorizing the work. Health, ability, ambition, industry and fair dealing were basic elements. The peculiar traits and capacities of the brothers were complementary. From the first, they were systematic in visiting medical centers and bringing back whatever was worth while, and in supporting organized medicine and attending society meetings, presenting papers and participating in the discussions. They were frequent visitors to the clinics of McBurney, Bull, Abbe and Weir in New York; Price in Philadelphia; Fenger, Ochs-

ner, Senn and Murphy in Chicago; Osler, Welch and Halsted in Baltimore; and Cheever, Warren, Cabot and Richardson in Boston. Constantly, they communicated to medical journals their experience, which was usually greater than that of others. They made full use of all ethically permissible methods of publicity, and were unfairly blamed accordingly. The financial return was large, but it is stated that 25 per cent of their patients paid nothing, 30 per cent paid the bare cost, and from 45 per cent came the professional fees, which in the end, in the form of endowments for research and education, were "turned back to the People from whom it came."

Miss Clapesattle, editor of the University of Minnesota Press, to whom the writing of the Mayo biographies* was entrusted, has produced a work—almost monumental in character—covering a far wider field than the biography of three physicians. Its pages represent prodigious bibliographic research, documented in a section at the end of the narrative text. Each phase of the career of the three doctors is pictured in a setting of the locale and contemporaneous events, affording a usually interesting and often very valuable historical background: the founding, in 1903, of the Society of Clinical Surgery—the model for all peripatetic clinical groups; the beginnings and course of specialization at the clinic, the additions to the staff, the growth of laboratory work, and the undesired publicity thrust on the brothers and the accusations of unethical conduct that beset them; and the part played by the clinic in World War I.

Among the million patients who passed through the Mayo Clinic, among the uncounted friends in and out of the profession, among students and historians of the medical scene, there will be thousands who will read every word of *The Doctors Mayo* with intense interest. For the average reader, both lay and medical, the book is too long, too detailed, too anecdotal, too full of trivialities. There are occasional lapses from the canons of good taste, occasional inaccuracies and interpre-

*Clapesattle, H. *The Doctors Mayo*. 822 pp. Minneapolis: University of Minnesota Press, 1941.

tations of dubious validity, and rare mistakes. But these criticisms are in themselves trivial, and one can only admire the work of Miss Clipesattle in her portrayal of these three beloved physicians.

MEDICAL EPONYM

SOUTHEY'S TUBES

These tubes are described by Reginald Southey (1835-1899) in the report of a case Chronic Parenchymatous Nephritis of Right Kidney. Left kidney small and atrophied—old scrofulous pyelitis, which was read before the Clinical Society of London on April 27, 1877 and which appears in the *Transactions of the Clinical Society* (10, 152-157, 1877). A portion of the article follows:

I determined to endeavour to relieve her dropsy by mechanical means and to this end employed an apparatus which is, I believe novel in England. I had a small trochar made with two well fitting canulas but little larger than the ordinary subcutaneous injection needles these canulas instead of terminating with a protecting rim and with a little bulbous extremity.

They are inserted into the subcutaneous cellular tissue with great facility and with no more pain than the ordinary needle prick produces. The canula inserted parallel to the surface is left stuck in the skin and a long fine capillary india-rubber tubing is now drawn over the protruding bulb and tied *in situ*. This tying in of the canula is not essential or even often necessary.

The long ends of the capillary tubes are now carried outside the bed and into a pan beneath it into which the serous dropsical fluid drip or drains away.

One drainage canula was inserted into each leg and through the two tubes about 2½ pints or in fact 71 ounces, of dropsical effusion drained away each 24 hours with considerable relief of course to the tension.

R W B

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON ARRANGEMENTS

Owing to the restrictions on gasoline and train travel and to the scarcity of hotel accommodations in Springfield, the Committee on Arrangements will recommend that the Council rescind its vote of May 25, 1942, whereby Springfield was designated as the place of the annual meeting in 1943. This committee will further recommend that the annual meeting in 1943 be held in Boston on May 25 and 26. Both recommendations have been endorsed by the Executive Committee.

GORDON M. MORRISON, *Chairman*

STATED MEETING OF THE COUNCIL

A stated meeting of the Council will be held in John Ware Hall, Boston Medical Library, 8 Fenway, on Wednesday, February 3, 1943, at 10 30 a m.

Business

- 1 Call to order at 10 30 a m
- 2 Presentation of record of meeting held October 7, 1942 as published in the *New England Journal of Medicine*, issue of November 12, 1942
- 3 Report of Auditing Committee and of Treasurer
- 4 Reports of standing and special committees
- 5 Appointment of Delegates
 - (a) To the House of Delegates American Medical Association, for two years from June 1, 1943
 - (b) To the annual meetings of the five New England state medical societies in 1943
 - (c) To the Annual Congress of the American Medical Association on Medical Education and Licensure at the Palmer House, Chicago February 12 and 16 1943
- 6 Such other business as may lawfully come before the meeting

MICHAEL A. TIGHE, M.D. *Secretary*

The two following reports are submitted for the advance information of members of the Council.

REPORT OF THE COMMITTEE ON FINANCE

The Committee on Finance, after some preliminary correspondence met on December 10, on which date the various committees are obliged by the by laws to have turned in their estimates for the coming year. There were present Drs. Charles F. Wilinsky, Peer P. Johnson, Ernest L. Hunt, Edward J. O'Brien and John Homans. The Treasurer, Dr. Butler, was prevented by illness from attending. His absence made much of our information concerning the expenditures for the past year uncertain.

The committee had been informed however by Dr. Butler that the income and expenses of the Society for the year 1942 were likely to balance fairly closely. In other words there was little likelihood of a favorable surplus such as had been secured in previous years. In 1942 the loss in dues owing to the entrance of members into the military services was beginning to be felt. But the Society should still have enjoyed an income from dues of something like \$55,000. To this about \$3,000 in income from invested funds should be added making roughly \$58,000 in all. Much of this is guesswork since the Treasurer's books are not made up until the first of the new year. Very likely if the income and outgo nearly balanced the income was considerably less, since the budget of \$50,800 could hardly have been overspent by any considerable amount. Owing to the establishment of the Blue Shield the Committee on Public Relations exceeded its budget by about \$1,000 and the Secretary was obliged to exceed his budget by over \$1,300 on account of the new by laws and other extras. However, the Committee on Arrangements made \$3,000, which more than balances these sums. The Committee on Publications,

ments and medications as prescribed and directed by a person licensed to practice medicine, and the application of such nursing practices and procedures as involve an understanding of cause and effect in order to safeguard the life and health of a patient and others.

In other words, she is a woman (or man) of good education who has been given three years of intensive training in the basic medical sciences and in the care of patients under the constant supervision of nurse educators, medical educators and interns. She is a woman of a certain maturity, responsibility and independence. These qualities make her desirable for Army service, where situations may arise that call for rigid discipline as well as judgment and initiative. She works best on acutely ill patients in hospitals and homes, and in executive and administrative posts in hospitals and public-health agencies, and as a staff nurse. Her shortcomings are those that might be anticipated because her experience is limited to work in large hospitals filled with surgical and critically ill medical cases; she is often unwilling or unable to do cooking and housekeeping (this fault is not confined to this class of nurse); she is unhappy in caring for patients with chronic disease and for well babies; and she shows signs of being a specialist.

Several estimates of the number of registered nurses in this country have been recently made. They vary considerably. No conclusion can be reached by adding up the number of graduates of nursing schools in the last twenty or thirty years for several reasons: some graduates (7 per cent or more) do not take or pass state registration examinations or National Red Cross standards; many get married (the marriage rate for all nurses under forty is 48.4 per cent); and a few abandon their careers for other types of work, although some return as their circumstances change or the demands for service increase. The most authoritative recent survey is the National Inventory of Registered Nurses in 1941, which was summarized in the *American Journal of Nursing* (42:769-773, 1942) by Pearl McIver. A questionnaire was sent to the 369,287 nurses listed in the 1940 census. Answers were received from 289,286, of whom 173,055 (60 per cent) were engaged in practice. If those who did not reply are rated as inactive, then only 45 per cent of the total number were active. However, of the 116,231 inactive nurses who returned their questionnaires, 25,252 (22 per cent) stated that they were available for duty in case of need. In other words, in January, 1941, there were 198,307 registered nurses active or available in the United States. Approximately 50,000 nurses have been graduated in the subsequent two years. A second inventory has just been authorized to bring the statistics up to date.

Of the employed nurses in the 1941 inventory, 81,708 (47 per cent) worked in institutions, 46,793 (27 per cent) were on private duty, 17,766 (10 per cent) were in public-health positions, 5512 (3 per cent) were in industrial plants, and the other 13 per cent held miscellaneous or undescribed jobs. Nurses who were unmarried and under forty years of age numbered 98,693. Estimating physical disabilities at 20 per cent, it was probable that at that time (January, 1941) there were 75,000 to 80,000 nurses available and acceptable for war duty. This number has been increased by the graduation of several classes since, and by the recent Army rulings that married nurses are acceptable if they are not with their husbands and if they are willing to go anywhere and that women up to forty-five years of age may be acceptable.

These statistics clearly show that there are enough registered nurses to meet the demands of our armed forces.

But they are not being met. Figures given out by Miss Marian G. Randall, chairman of the Inventory Committee of the governmental Subcommittee on Nursing, showed 30,000 nurses in the Red Cross First Reserve in April, 1942. The monthly quota of 3000 since that time has not been reached. How serious the deficit is cannot be estimated, for exact figures are withheld on grounds of military expediency. The various states, in April, 1942, had contributed from 13 to 60 per cent of their quotas; Massachusetts was credited with 1206, or 20.5 per cent of its quota.

The military authorities are disturbed by this inadequate response. The American Nurses' Association, in co-operation with the League of Nursing Education and the Red Cross Nursing Service, early last year set up a committee, known as the Nursing Council on Defense, in each state. Since Pearl Harbor, the title has been changed to Nursing Council for War Service. These committees have been very active in securing nurses for the Army and Navy and in aiding in the major readjustments that have been forced on civilian hospitals, industrial plants and public-health and civilian-defense agencies. However, they do not have enough power to be effective. A serious shortage of nurses is reported from various parts of the country. The average hospital has lost only three or four nurses; but many state and mental hospitals and some metropolitan hospitals have suffered severely. Moreover, population shifts resulting from the establishment of war-industry plants have not been met by changes in nursing ratios.

The problem has many sides and is being met by a number of solutions. An obvious first step is now under consideration — that of fashioning an agency with power to induce nurses who should join the armed forces to do so, and with power to allocate important nursing teachers, supervisors and administrators to their jobs so that essential teaching and hospital services will not be stripped. Another step that provides quick results is the recall of inactive nurses. As noted above, more than 25,000 trained women indicated last year their willingness to return to duty should the need arise, and they are doing so. More than 700 have come back in Massachusetts, and the Committee on Public Safety, in co-operation with nurses' organizations, is striving to get others. It is obvious that service means dislocation of family life and jobs to many of them. Some are serving at considerable personal sacrifice; others can give only part of their time. The same is true for those who are handicapped by physical or age infirmities. Hospitals gladly make allowances for such factors. For those who need to brush up on recent nursing procedures, refresher courses have been given with federal grants-in-aid. More than 500 have attended courses in this state in the past year. However these re-activated nurses can take care of only a small fraction of the present deficit. It is clear that more nurses must be trained, as many and as soon as possible.

There has been a marked increase in the number of pupil nurses in accredited nursing schools in the United States in the last few years. There were about 79,000 of them in 1929, an average of 70,000 yearly in the next decade, and then a rise to 82,000 in 1939, 85,000 in 1940, 87,588 in 1941, and 91,457 in January, 1942. Thus there has been an increase of 11 per cent since 1939. Admissions in 1942 have been approximately 49,000, or 18 per cent more than in 1941. But authorities in Washington had set 55,000 admissions as the goal for this year. It was not reached in spite of an intensive campaign of adver-

tising and interviews in schools and colleges Does this mean that only 50,000 young American women can be yearly induced to take up nursing? Some nurse educators are inclined to believe that this is a saturation point for the profession Or does it mean that many who might enroll do not yet realize the need for nurses? Or that they are more attracted to the WAACs and the WAVES and defense industries, which have more to offer financially and patriotically in immediately useful war work?

Answers to these questions will influence greatly the educational plans now under advisement Schools of nursing have been criticized for rejecting applicants on the ground that unduly rigid entrance standards are responsible for the shortage of pupils That this is not so is shown by the fact that about one third of the women who enter nursing schools leave before their three years are up, according to figures published in the pamphlet "Facts about Nursing" issued by the Nursing Information Bureau in 1941 It appears that the greater part of this considerable wastage represents changes in career (marriage, industry) Scholastic failures are relatively few More lenient admission policies would undoubtedly only increase the wastage With the continuance of this loss, it is estimated that 26,000 to 28,000 nurses will be graduated in each of the years 1942 through 1944 Surely the totals are not large enough to warrant optimism concerning their adequacy in meeting the Nation's needs for war and for the care of the civilian population

A few remarks on nursing schools may be pertinent at this point There are 1300 accredited nursing schools in the United States They are run by educators of ability, and they have drawn freely from the pedagogical wisdom of schools and colleges Their standards are subjected to frequent review by the National League of Nursing Education and the state boards of nurse registration Legal requirements for registration of graduates are quite uniform Good moral character is universally demanded Four years of high school is preliminary educational background required by forty-four states Training must be of three years duration in forty-three states, but fourteen (including Massachusetts) allow six to twelve months' credit for college work Age at registration must be at least twenty-one in forty-three states The structure of the courses and the requirements for practice are the outgrowth of many years of experience on the part of those who have worked constantly with nurses Therefore any suggestions concerning their alteration because of the war emergency should get the consent and co-operation of informed sources before they are put into effect

An increase in the number of training schools waits on proof that existing schools cannot take care of the applicants for admission and on proof that the proposed new schools can provide facilities for turning out graduates acceptable to the boards of registration The trend of the past decade has been toward fewer and better schools similar to the trend in medical schools a generation ago Schools have been asked to admit three classes annually as another way of accelerating production Naturally the decision to do so must rest with the individual school according to the best method it finds of handling its teaching housing its students and caring for its hospital patients

We have listened to much criticism of the registered nurse and her school We are told that she knows both too much and too little that she wants to be a specialist that she dislikes work outside hospitals, that she is unwilling

to do housework and cooking and so forth All of us have had disagreeable experiences with this sort of nurse Nurse educators freely admit her existence We have also heard it asserted that schools teach much that is unnecessary, beyond the pupil's grasp and in a too rigid and complex fashion Again, responsible nurse educators agree in part, and point to their frequent consultation with pedagogical experts and their constant revision of curriculums Recently in this state a review of the contents of the various courses was begun at the direction of the State Board of Nurse Registration and the Nurses Association and with the advice of physicians in the several specialties But does it follow that better nurses can be produced if they are not taught so much and in a shorter time?

It does not seem wise to lower the entrance requirements for pupil nurses, for a high school background is essential, and a college course desirable if they are to absorb the training that they are offered Furthermore the quality of a product depends not only on the quality of the material that is put into it but also on the time that is allowed for its growth Judgment medical in sight and discipline take time to ripen More can be expected of a nurse trained for three years than of one trained for one year Nurses are what they have become today not because they have banded together in an exclusive guild that relegates the interests of patients and physician to a position below their own They are what their employers the physicians, have helped them to be The medical profession has fostered their development as nurses theists, operating room assistants, administrators and research aides every year it adds to their tasks more tests and treatments that doctors only were accustomed to perform This tendency has increased as the shortage of physicians has grown and nursing schools must continue to supply the demand Military authorities show their approval by accepting only the three year trained nurse Nurse educators resist the demand for thoughtless mass production, pointing to the unfortunate situation that followed World War I when many hastily trained nurses were thrown on the market who, unable to meet the requirements of boards of registration practiced an inferior brand of nursing that reflected on the profession and themselves English representatives who have seen their country struggle with a mass of volunteer and partially trained workers in the last three years have urged us not to lower our standards for those who must supervise auxiliaries

It comes down to this — one type of nursing school can not produce all types of nurses Nurses for general and home duty can be trained in a year or so by schools for licensed attendants as discussed in the next section Nurses for special hospital and war service must continue to be trained by the schools of nursing No shortening of the duration of their course should be recommended since this would interfere seriously with the quality of the graduates The three year course cannot be condensed by the elimination of vacations as the medical school course has been for nurse pupils get only three weeks vacation each year We do not feel competent to pass judgment on the possible elimination of subjects or of hospital affiliations for the same purpose but we can see disastrous effects on hospitals that have come to rely on the services of pupil nurses in the care of their patients if those services are taken away from them The League of Nursing Education aware of the critical shortage of nurses and the factors discussed above has made certain suggestions in co-operation with the Office of Civilian Defense and

the Sub-Committee on Nursing in Washington. The following is quoted from the *American Journal of Nursing* (42:1182, 1942):

While emphasizing the importance of maintaining adequate preparation, the Board [of Directors] recognizes that civilian hospitals are becoming more and more dependent on student nurses to care for their patients and to be ready for civilian emergencies. In view of this situation, therefore, the Board recommends:

1. That schools offering the three-year curriculum plan to complete within thirty months all organized instruction and clinical experience in at least the four major services, medicine, surgery, obstetrics and pediatrics, leaving six months free for supervised practice wherever needed in the hospital. This arrangement would also make it possible, should a plan be worked out in co-operation with Army and Navy hospitals, for students who choose to go into military service, to have such an affiliation during this six months; or later if the need becomes more acute, students might be released to enter military service at the end of 30 months.

2. That, where state laws permit, an accelerated program be planned for students admitted with two to four years of approved college preparation which would make it possible for such students to graduate at the end of 24 to 28 months. The length of time should be determined on the basis of the previous educational preparation of the student and her level of achievement in the school.

3. That schools of nursing critically examine their curricula and eliminate duplication in instruction and non-essential activities, giving emphasis to those elements in the curriculum that are most vital in terms of present and probable future needs.

4. That every effort be made to extend the use of auxiliary personnel in so far as this can be done with safety to the patient.

5. That in view of the greatly enlarged numbers of student nurses and auxiliary personnel in hospitals, definite measures be taken to retain and stabilize teaching and supervisory staffs to provide for the adequate preparation of students and the proper supervision of auxiliary workers.

A few final comments on the efficient use of the present store of nurses remain. Private-duty nurses must be prepared to render any service necessary in homes. "Luxury nursing" is out for the duration of the war. Patients must accept the decision of the hospital administrator and the clinical staff whether they need special nurses, and for how long, regardless of their ability to pay. The sharing of a special nurse by several patients has been tried and the experiment has failed, owing to personal difficulties. Hospital authorities have been asked to "alter their personal policies in ways which will encourage graduate nurses to remain in institutional service." This is a cautious expression of the fact that hospitals must pay their nurses enough to meet the competition of industrial nursing and non-nursing war work. Furthermore, the Congress of the United States appropriated \$1,800,000 in 1941 and \$3,500,000 for 1942 and 1943 for nursing education, these funds to be used to assist nursing schools to expand their teaching facilities and as scholarships for young women needing financial aid in undertaking a professional course.

Licensed attendants. A licensed attendant is defined in the law (Chapter 620) enacted in Massachusetts in

January, 1942, as one whose purpose is "to care primarily for convalescent or chronically ill patients or those suffering from minor ailments, in hospital or home, under the supervision and direction of qualified physicians" and "to assist registered nurses in the care of acutely ill patients in hospital or home, under the supervision and direction of qualified physicians." This law attempts to regularize a miscellaneous group of nurse workers for the protection of the public. Some are graduate nurses who did not take or failed to pass registration examinations; others are graduates of unrecognized schools of nursing or graduates of good schools of practical or household nursing, or women self-taught or sketchily trained in nursing homes. All of them could be licensed to practice if they passed the state examination for licensed attendants by August, 1942; since that time, they must show that they have been graduated from attendant nurse schools approved by the state nursing authority. Since registration is so recent a development, there are no reliable figures concerning the number of these nurses in the United States that can be used as an estimate of the aid which they can give in the present emergency.

The foregoing definition shows that the licensed attendant is designed to supplement the services of the registered nurse and to render those that the registered nurse does not. She must know how to cook and how to manage a household; she must have the humility to be content with caring for patients with minor illnesses and for well babies; and she must have the patience and persistence to serve chronically ill or elderly patients for months or years. To fulfill these duties, she does not need to have as much preliminary education or as much training in school and hospital as the registered nurse. While her weekly wages are less than those of the three-year nurse, her annual income is often as great or greater. Practicing physicians know her value; in fact, they really prefer her services when they have problems such as those listed above. Leaders of the nursing profession also recognize her worth and have sought for many years to establish her on the sound educational and legal basis that has now been effected.

Reasons for the tardy recognition and utilization of the attendant nurse are many. An irritating but minor one is her competition with the private-duty nurse. It would seem that physicians could lessen this by a wise choice of the type of nurse they need for any particular case, and that nurses could do their part in fostering co-operation by granting the licensed attendant some degree of participation in the American Nurses' Association. Such a step would go far in promoting mutual understanding and respect and make less likely the development of a rival organization with contests concerning fields of interest. Large metropolitan hospitals have long refused to employ attendant nurses because they are not trained adequately to serve seriously ill patients and because pupil nurses can render all necessary services to the rest. Now, however, hospitals are so short of staff nurses that they have begun to use attendants on certain wards and in certain situations, and on the whole, the experiment seems to be working well. Emergency medical units and the hotel hospitals now organized by the Office of Civilian Defense include licensed attendants. Veterans' Administration hospitals should find many places for them. Public-health nurses are finding them useful in extending their services. It is likely that military authorities will be forced to call on them for work in their hospitals for wounded soldiers and sailors to relieve corps men. So it is obvious that a broad career is opening up for the licensed attendant.

Nevertheless, her chief usefulness, and her chief interest to us at this time, is in civilian community service, for in case of disaster or epidemic, the bulk of the medical work will be done in homes.

There are now in Massachusetts eight schools for attendant nurses—Beverly Hospital, Harley Hospital, Household Nursing Association, Holden District Hospital, North Adams Hospital, Tewksbury State Hospital, Waltham Training School, and Robert Breck Brigham Hospital. There are three types of setup for such schools. One is quartered in a chronic hospital (such as Tewksbury) with a practice house on the grounds for training in home cooking and management. Another is centered on the public school system (as in the Rochester, New York experiment). The third, which appears best, is that of the Household Nursing Association, which gives two months of preliminary training in its central group of buildings, affiliates with a number of small neighboring hospitals for twelve months of ward work, and then supervises work in actual homes for six months. The Massachusetts Approving Authority demands a minimum of twelve months training. All these establishments are relatively inexpensive and should be multiplied throughout the State.

Long before Pearl Harbor, the far-sighted management of the Household Nursing Association made efforts to increase their enrollment. Their capacity with seven classes a year was 168, and their average pupil census was 125. They found that they could double this number without extending the hospital affiliations. The hospitals were so eager to secure the services of the pupils that they offered to pay the \$60 tuition for all applicants who could not afford it. Yet their enrollment did not increase, in fact, there were, at the end of November 1942, only 5 applicants for the December class, which normally numbers 18. They redoubled their efforts, with the aid of the Committee on Public Safety, and by advertisements and articles in newspapers, the radio and schools, with scanty results. As an example, one newspaper story netted several hundred replies, out of which came forty interviews and finally two unattractive applicants. Commissioner Downey informs us that efforts were made, a year ago, to enlist attendant nurse pupils by talks by teachers and personnel advisers in various high schools throughout the State, but that the experiment was such a failure that it has not been continued. The Waltham Training School may be forced to close for lack of pupils, and the other schools are similarly affected. What are the reasons for this general lack of interest on the part of young (and middle-aged) women in attendant nursing? Are they not sensitive to calls for patriotic and community service? The most likely answer is that they can get better pay and more attractive work and hours in stores and manufacturing plants, which are calling even more loudly for them.

Certainly leaders have proposed that, in view of the country's urgent need for nurses, we should concentrate on the development of the licensed attendant in all hospitals qualified to teach. They assert that these women can give satisfactory service and that hospital nursing and military authorities should be forced to conform before it is too late. The proposals have been approved by some physicians and are the reason for this general report. The Committee on Medical Education finds them unsound on several counts. The most insurmountable obstacle right now is the failure, after considerable effort, to fill already established attendant nurse schools, as noted above. Perhaps this could be done by some form

of the draft to which women are not as yet subject. But we doubt the workability of any scheme that would force people to perform tasks in which they are not interested. It might be that a section of the WAACs and the WAVES could be allocated for nurse training and duty in special situations; it would be hard to apply them to civilian use. It is stated that more candidates could be obtained if they had the opportunity to train in large metropolitan hospitals. Attendant nurse educators do not believe this. Furthermore the quality of service that can be rendered by an attendant nurse is adequate only for chronic cases, the elderly, the well babies and children, and for simple household situations. We know that five-minded, eager women can be taught in a very short time to give excellent auxiliary aid and even to perform difficult nursing, medical and laboratory procedures. Such training requires a great deal of individual effort and supervision. The average pupil and the average class in any program of mass production respond to a much lesser degree, hence the necessity for the three-year program for turning out workers who can serve in acute medical and surgical cases and in military situations. Attendant nurse and registered nurse educators and hospital executives all agree that to use attendant nurses for cases beyond their ability is a sure way to invite disaster. Finally the establishment of two types of nursing schools in one institution is hazardous. The content and scope of the courses are necessarily different, so is the type of work on patients, and all this would lead inevitably to social and professional jealousies and friction no matter how good the behavior of all, and impose a heavy additional burden of teaching and supervision on staffs that are straining every nerve to turn out the essential graduate nurse.

For Cross volunteer aides. In 1941 the American Red Cross and the Office of Civilian Defense arranged a program for the training of volunteer nurses aides. As it now stands it gives women who are American citizens of good character and between the ages of eighteen and fifty who have had a high school education and who are physically fit and able to stand hard work one hundred hours of training. Half this time is spent in classrooms, and half in hospitals under the supervision of nurses. After completing the course, the aides buy their uniforms and promise to serve a minimum of one hundred and fifty hours each year for the duration. Hours are quite elastic and not necessarily in one continuous stretch. In time of crisis it is understood that the service may be longer and may be called for at distant points. It is women such as these (140,000 of them) that helped England immeasurably in these last three years. It was hoped that 100,000 of them might be trained in this country by the end of 1942. Actually this goal has by no means been reached (about 4000 exist in Massachusetts). Yet the results have been extremely gratifying from many points of view. About five hundred training chapters are functioning throughout the country, seventy-one hospitals are now teaching or available for teaching in Massachusetts. These volunteers are coming largely from an older group of women. They are wives and sisters of men in service, some are doctors' wives, schoolteachers and business women. They take their work seriously, glamour girls do not last. They have won the respect and admiration of nurses. Hospitals are eager to get them. They have done much for patients. They have become interpreters of medical, hospital and nursing needs to the community. They will be a real source of help in case of disaster or

difficulties arising from the loss of trained nurses to the armed forces. They are to be complimented and encouraged in every way.

Ward helpers. Ward helpers act as ward maids and run errands for patients and nurses. As the shortage of nurses has developed, they have been given minor duties in the care of patients. Essentially their jobs are similar to those of the Red Cross volunteer aides. They are more reliable for routine daily service because they are paid. It is foreseen that situations might arise calling for regular work on the part of the volunteers that they could not afford to give without recompense, since to do so would mean the loss of jobs or the disruption of family responsibilities. Therefore it is agreed that the volunteers may, in such circumstances, be paid, suffering thereby the loss of their uniforms and their amateur standing. Ward helpers usually are trained in the hospitals where they work. They can also be obtained from the Household Nursing Association, where they are given a one-month preparation course.

Ward helpers obviously are valuable to institutions but do not meet other community needs. To supplement the services of nurses and attendants in homes it is proposed that women able and willing to do household tasks freely or for hire, sign up with some central office, such as a nursing registry or a public-health agency. The proposal is certainly worth attention, although it is hard to guess what the response would be.

ROBERT T. MONROE, *Chairman*

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

ECTOPIC PREGNANCY

As has been customary in previous analyses, all cases of ectopic pregnancy are grouped under this specific heading, although in one sense they are surgical complications. There were 6 maternal deaths due to ectopic pregnancy during 1941, twice as many as occurred in 1940. One autopsy was performed.

The first case was that of a thirty-six-year-old primipara who began to stain when about two months pregnant and continued to do so for one month. She had had attacks of knifelike pain in the lower abdomen for the two weeks prior to hospital entry, and vaginal examination on admission showed that definite placental tissue was extruding from the os. A moderate amount of this tissue was obtained by curettage, and a firm mass was found in the anterior cul-de-sac, for which nothing was done. The following day the patient went into shock, and at laparotomy, the abdomen was full of blood, the bleeding arising from what was apparently a ruptured left tubal pregnancy. There was a hematosalpinx on the right. Bilateral salpingectomy was performed. Peritonitis developed and death resulted. Autopsy showed extensive hemorrhagic peritonitis. The ruptured tube did not reveal gross or microscopic evidence of ec-

topic pregnancy. This case was an unfortunate one. Intrauterine and extrauterine pregnancy existing at the same time are not uncommon; neither is it uncommon to have a ruptured tube due to ectopic pregnancy reported negative by the pathologist. Had this patient been operated on the day of the curettage, before rupture of the tube had taken place, in all probability the fatality would have been averted.

The second patient was a forty-three-year-old woman whose history is most inadequate so that her parity is in doubt. She was seen first when in a state of collapse and shock from abdominal hemorrhage; she was taken to the hospital by ambulance and died a few minutes after entry. The diagnosis of ectopic pregnancy with massive abdominal hemorrhage is probably the correct one; however, the medical examiner, who is said to perform no autopsies himself, refused autopsy in spite of the requests for one by the patient's physician and by the superintendent of the hospital where she died. One of the striking deficiencies of medicine in Massachusetts that has been brought out by the maternal mortality study is the attitude of some of the medical examiners toward performing autopsies on patients who die in childbirth.

The third patient was a twenty-seven-year-old primipara who was seen by her physician because of sudden severe pain in the right lower quadrant. Physical examination was negative. The pain increased during the next few hours, and the abdomen became distended; the patient went steadily downhill and died at home before the ambulance arrived. The diagnosis of ectopic pregnancy, as in the previous case, is the probable one; however, as neither operation nor autopsy was performed, it cannot be confirmed. In the absence of nausea and vomiting, and in view of symptomatology of so few hours' duration, hemorrhage was the most likely cause of death, and ectopic pregnancy the probable source of the hemorrhage.

The fourth patient, a thirty-eight-year-old multipara who had had one abortion at five months, was seized with sudden pain in the lower abdomen, accompanied by vaginal bleeding, when approximately eight weeks pregnant. After consultation, ruptured tubal pregnancy was diagnosed, and at operation the left tube was found to be ruptured and was removed. The patient was given one transfusion of 500 cc. of citrated blood, in spite of which she died about five hours after operation. Delayed operation was not a factor in this case, since the patient was operated on soon after the diagnosis had been made; it is possible that additional transfusions might have averted the catastrophe.

The fifth patient was a thirty seven year old mul-
tupara on whom operation for repair of a rectocele
and fixation of the uterus was performed. At
operation a mass on the right side was found,
which was said to have been a tubal pregnancy.
Following this operation the patient became anuric
and died. The description of the operation states
that the uterosacral ligaments were plicated, and
in all probability both ureters were involved in
this operation, thus causing the anuria. Although
this death is attributed to extruterine pregnancy,
which was an incidental finding at operation, the
true cause was bungling surgery.

The sixth and final case was that of a thirty nine
year-old primipara who was hospitalized for ob-
servation because of vaginal bleeding. Because the
red cell count fell very materially, operation was
decided on. Ectopic pregnancy was found, and
both tubes were removed because of extensive
adhesions. The patient died three days later,
probably because of bronchopneumonia. There is
little to be said about this patient, she was appar-
ently doing well from the surgical standpoint but
expired because of a respiratory infection.

The two patients who died without operation
show how serious the result of hemorrhage may
be and how important it is that operation be per-
formed whenever the diagnosis of ectopic preg-
nancy is suspected. This is the only way in which
such fatalities can be prevented.

DEATHS

PETERSON — JOHN A. PETERSON, M.D. of Hingham
died December 26. He was in his seventy third year.

Dr. Peterson attended Powers Institute and received his
degree from the University of Vermont College of Medi-
cine in 1896. For four years after his graduation he prac-
ticed in Guilford, Vermont. He then went to Hingham.
He was former medical examiner of the Fifth Plymouth
District and a former member of the Massachusetts Medi-
cal Society and the American Medical Association.

His widow and a daughter survive him.

STICKNEY — EDWIN P. STICKNEY, M.D., of Arlington
died January 8. He was in his eighty first year.

Dr. Stickney received his degree from Harvard Medical
School in 1892. He was a fellow of the Massachusetts
Medical Society and the American Medical Association. He
was also a member of the New England Pediatric Society
and the Arlington Doctors' Club.

Two daughters, a brother and three grandchildren sur-
vive him.

MISCELLANY

ELLA SACHS PLOTZ FOUNDATION

During the nineteenth year of the Ella Sachs Plotz
Foundation for the Advancement of Scientific Investiga-
tion forty four applications for grants were received by
the trustees, thirty six of which came from the United

States, the other eight coming from six different countries
in Europe, Asia and North and South America. The total
number of grants made during this year was twenty six,
one of these being a continued grant.

In the nineteen years of its existence the Foundation
has made four hundred and fifty five grants to scientists
throughout the world.

In their first statement regarding the purposes for
which the fund would be used, the trustees expressed
themselves as follows:

For the present researches will be favored that are
directed toward the solution of problems in medicine
and surgery or in branches of science bearing on
medicine and surgery.

As a rule preference will be given to researches on
a single problem or on closely allied problems. It is
hoped that investigators in this and in other countries
may be found whose work on similar or related prob-
lems may be assisted so that more rapid progress may
be made possible.

Grants may be used for the purchase of apparatus
and supplies that are needed for special investigations
and for the payment of unusual expenses incident to
such investigations including technical assistance but
not for providing apparatus or materials which are
ordinarily a part of laboratory equipment. Stipends
for the support of investigators will be granted only
under exceptional circumstances.

In the past few years the policy outlined in the second
paragraph has been neglected. During the present great
need for funds grants will be given in the sciences closely
related to medicine without reference to special fields. The
maximum size of grants will usually be less than \$500.

Applications for grants to be held during the year
1943-1944 must be in the hands of the Executive Com-
mittee before April 1943. There are no formal applica-
tion blanks but letters asking for aid must state definitely
the qualifications of the investigator, an accurate descrip-
tion of the research, the size of the grant requested and
the specific use of the money to be expended. In their
requests for aid applicants should state whether or not
they have approached other foundations for financial as-
sistance. It is highly desirable to include letters of rec-
ommendation from the directors of the departments in
which the work is to be done. Only applications comply-
ing with the above conditions will be considered.

Applications should be sent to Dr. Joseph C. Aub, Mas-
sachusetts General Hospital, Fruit Street, Boston.

CORRESPONDENCE

EXPECTORANTS

To the Editor: I have been interested in reading in
the September 3 issue of the *Journal* the article on virus
pneumonitis by Drs. Dingle and Finland. There is one
point brought out by these authors to which I wish to take
exception. On page 394 they say: "Expectorants may
be helpful when sputum is scant. If they refer to the
commonly used stimulating expectorants which act by
virtue of the fact that they are excreted in the bronchi, the
use of such drugs seems irrational. They are supposed to
increase secretion by acting as irritants to the mucous
membranes where they are excreted. To irritate further
an already inflamed mucous membrane does not seem
likely to add to the comfort of the patient."

I am strongly inclined to believe that expectorants so used tend to increase cough in the acute stages of respiratory infections, and I have seen a number of cases of persistent cough and subacute cases that were promptly relieved when the patient stopped taking the expectorant.

GEORGE C. SHATTUCK, M.D.

25 Shattuck Street
Boston

* * *

Dr. Shattuck's letter was forwarded to Dr. Finland, whose reply is as follows:

To the Editor: According to my understanding, it is the purpose of an expectorant to decrease the viscosity of sputum and make it easier to raise, thus indirectly relieving the marked irritation that results from the difficulty in dislodging thick tenacious sputum during cough. Further relief from the irritation may be sought through the administration of generous doses of codeine or of suitable doses of such drugs as Dilaudid, if necessary. There is evidence to indicate that the viscosity of the tracheo-bronchial exudate is decreased by the usual expectorants and by the inhalation of moist air or mixtures of oxygen and small concentrations of carbon dioxide or compound tincture of benzoin (Basch, F. P., et al. *Am. J. Dis. Child.* 62:981-990 and 1149-1171, 1941, and *J. A. M. A.* 117:675-678, 1941; Nelson, E. E. *Internat. M. Digest* 40:183-185, 1942).

Dr. Dingle and I were only too well aware of the frequent ineffectiveness of the usual measures. It must be borne in mind, however, that they are undertaken in the first place because the symptom is troublesome. Although Dr. Shattuck's experience may not be unique, the reverse is probably more frequently observed: that is, expectorants are withheld because relief from their use is not anticipated. The physician finally prescribes them in desperation, after which the patient begins to raise sputum more easily and with less irritation. Both these circumstances may, of course, be merely coincidences in the natural course of the disease. Two things are certain: severe and irritating cough is one of the most troublesome features of the prevalent primary atypical pneumonias, and the relief of this symptom is very difficult.

MAXWELL FINLAND, M.D.

Boston City Hospital
Boston

APPROVED LABORATORIES

To the Editor: In the October 8, 1942, issue of the *Journal*, a communication from this department was printed giving a list of the laboratories approved for performing premarital and prenatal serologic tests for syphilis.

Four laboratories have been added to this list, which brings the total to thirteen. The list is as follows:

State Wassermann Laboratory, Boston
Boston Dispensary, Boston
Boston Health Department, Boston
Leary Laboratory, Boston
Massachusetts General Hospital, Boston
Peter Bent Brigham Hospital, Boston
Health Department, Brockton
Truesdale Hospital, Fall River
Providence Hospital, Holyoke
St. Luke's Hospital, New Bedford
St. Luke's Hospital, Pittsfield
Mercy Hospital, Springfield
St. Vincent Hospital, Worcester.

Those sending such specimens to laboratories are reminded that no other laboratories in the State are approved for performing these tests.

PAUL J. JAKMAUH, M.D., *Commissioner*
Department of Public Health

State House
Boston

BOOK REVIEW

Manual of Standard Practice of Plastic and Maxillofacial Surgery. Prepared and edited by the Subcommittee on Plastic and Maxillofacial Surgery of the Committee on Surgery, Division of Medical Sciences, National Research Council, and representatives of the Medical Department, United States Army: Robert H. Ivy, M.D., chairman; John Staige Davis, M.D.; P. C. Lowery, M.D.; Joseph D. Eby, M.D.; Ferris Smith, M.D.; Brig. Gen. Leigh C. Fairbank, Medical Department U. S. A.; and Lt. Col. Roy A. Stout, D. C., U. S. A. With contributions of John Scudder, M.D., and Frederick P. Haugen, M.D. 8°, cloth, 432 pp., with 259 illustrations. Philadelphia: W. B. Saunders Company, 1942. \$5.00.

The purpose of publishing a series of manuals on military surgery, of which this is the first one, is to present in compact form essential up-to-date and reliable information regarding military surgery to medical officers who are, by necessity, called on to treat the wounded under adverse conditions, as specialization cannot be followed to the same degree in military service as in civilian life. The degree of success of such a manual is proportional to the fulfillment of the above purpose, and so far as this book is concerned, the reviewer believes that it has fulfilled this requirement to a great degree.

The book is divided into four sections: reconstructive surgery (250 pages); maxillary surgery (79 pages); maxillofacial prosthesis (34 pages); and anesthetic technics (22 pages).

The section on reconstructive surgery is the most ambitious and thorough chapter. The author covers almost the entire field of plastic surgery. One is particularly impressed with the careful selection of plastic procedures, and the rejection of many complicated and unavoidable operations. It is well for military surgeons to pay special attention to the "don't's" that the author courageously emphasizes throughout the text. The greater part of this section is based on civilian types of injury. Although these are very useful and will undoubtedly act as a guide for the treatment of gunshot wounds, one would wish that the author had utilized part of the vast material published on this subject during World War I.

The section on maxillary surgery lays special emphasis on the early treatment of fractures, and outlines many useful suggestions and aids for emergency and first-aid immobilization of fractures.

The least impressive part is the section on maxillofacial prosthesis. It gives very little that the military dental surgeon can utilize for the treatment of the wounded.

The fourth section comprises two short chapters on the application of local and general anesthesia.

The book is well edited and contains many excellent diagrams and illustrations. It will undoubtedly be a useful reference book for those who are assigned to treat injuries of the face and jaws, as well as general injuries.

(Notices on page x)

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DISSOLUTION OF PHOSPHATIC URINARY CALCULI BY THE RETROGRADE INTRODUCTION OF A CITRATE SOLUTION CONTAINING MAGNESIUM*

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BOSTON

IN a previous communication¹ from this clinic the possibility of using an isotonic citrate solution at a pH of 4.0 to dissolve urinary calculi was discussed and the successful treatment of one case of bladder stones by this method was reported. It soon became apparent that this solution was too irritating for routine clinical use, it is perhaps of historical interest that the patient who had been successfully treated for bladder stones had a so called "cord bladder" and hence was not disturbed by the irritation. Furthermore, if citrate solutions by irritation give rise to bleeding, this continues since the citrate prevents coagulation of blood. A study was therefore undertaken to find a solution that would be not only effective in dissolving calculi but less irritating.

The speed with which various solutions dissolve calcium phosphate calculi was quantitated by the speed with which they decalcified rabbits' teeth², the irritability of the solutions was studied by noting their effect on the mucosa of rabbits' bladders³. A large number of organic acids were tried; the effect of pH, tonicity, temperature, pK of the calcium salt of the acid and so forth were studied; some of the underlying laws were formulated⁴, and finally an isotonic solution of levulinic acid at a pH of 4.0 was selected. This solution was found to be less irritating, albeit considerably less effective, than the original citrate solution. The net result was an improvement, however, and several successful clinical experiences were obtained.

At this juncture it was discovered that the addition of magnesium ions markedly reduced the irritability of levulinic solutions⁵, the same was found to be true for citrate solutions and they were once more taken up for clinical use. The

present paper is concerned with a report of the dissolution of phosphatic stones in patients in whom a citrate solution containing magnesium ions (Solution G⁶) was employed.

CLINICAL MANAGEMENT OF CASES

Infection

In most cases during the dissolution the patients received moderate doses of sulfathiazole or a similar drug to prevent infection if it was not present, or to reduce it if already present.

Apparatus

The main object, of course, is to keep the solution in contact with the stone as much as possible. The actual apparatus used in each case depended on whether one was working through a simple nephrostomy tube, a two way nephrostomy tube, two nephrostomy tubes, a ureteral catheter and a nephrostomy tube, or one or more ureteral catheters. Technical aspects also varied depending on the degree of patency of the ureter and on how irritable the bladder and urethra were. Solution G is somewhat irritating, and some patients developed bladder symptoms if the solution was allowed to come out through the bladder, whereas others did not. Cases 3 and 5 illustrate how this difficulty was overcome.

When the stones lie in the kidney calyces it is desirable that a slight amount of intrapelvic pressure be obtained to make sure that the solution gets around all the stones. However, the operator should see to it that this pressure is not continuous lest a constant back pressure stir up a pyelonephritis. This means that the solution must in some way be introduced intermittently. Figure

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The formula of Solution C is as follows:
Citric acid (monohydrated) 3.75 gm
Magnesium oxide (anhydrous) 6.25 gm
Sodium citrate (anhydrous) 4.37 gm
Water q. s. ad 100.0 cc

1 illustrates one possible apparatus to obtain these ends.

With rare exceptions it is better that the fluid should not go in and out of one tube, as in the Munro⁵ tidal-drainage apparatus devised for irrigating so-called "cord bladders." The objection to such an apparatus arises from the fact that the

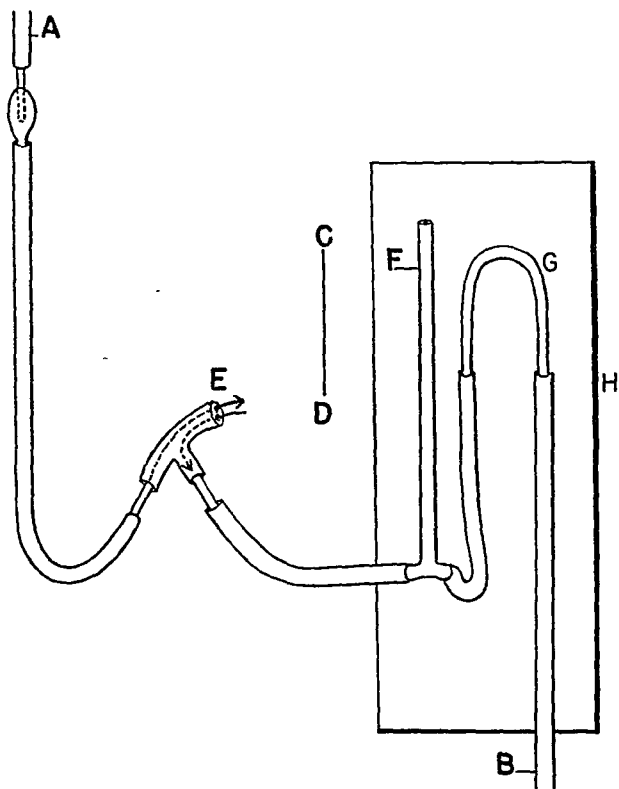


FIGURE 1. Tidal-Drainage Apparatus to Produce Intermittent Intrapelvic Pressure through a Two-Way Nephrostomy Tube.

A—tube from reservoir of fluid leading to Murphy drip; B—tube leading to waste-fluid; C—level where siphoning begins; D—level of pelvis; E—two-way nephrostomy tube leading to kidney pelvis; F—upright glass tube open at upper end; G—curved glass tube acting as siphon; H—board to which apparatus is fixed.

As fluid enters the system from A, the pressure rises until the fluid reaches C, the height of the siphon; at that point, fluid siphons off until air coming into tube F breaks siphon; the whole process then starts over again. The distance, C to D, measures the extent of intrapelvic pressure before the fluid siphons off.

dead space in the tubes is so great in comparison with the cavity being irrigated that a large proportion of the fluid that comes out of the cavity goes back into it again. The efficacy of such a system depends on the ratio of the volume of the viscus being irrigated to the volume of the dead space (tidal fluid). The Munro apparatus is very satisfactory for bladders but not for kidney pelves. If one cannot have a two-way drainage, as for example, when one is working through a ureteral catheter, it is necessary to inject the solution man-

ually into the end of the catheter or to use the alternate apparatus, devised by our colleague, Dr. Lawrence Kinsell, and shown in Figure 2. With the latter the constant presence of an attendant is required; this attendant can, however, be the patient himself.

If one is dependent entirely on the ureter for the introduction of the fluid, it is preferable to use a soft-rubber catheter (Bardam No. 10) because of the danger of erosion of the ureter after prolonged intubation with a hard-woven catheter. This soft catheter can best be introduced with the help of a fiber stylet; once in position it can be left for weeks (Case 6) or months, if one is to judge by experience with ordinary skin ureterostomies. The problem of keeping the ureteral catheter in place is a somewhat difficult one because of the tendency of the peristalsis of the ureter to displace it. This trouble has been overcome by the apparatus shown in Figure 2.

Evaluation of Results

For following the progress of dissolution and for determining just where the stone is in relation to the pelvis of the kidney, and hence whether fluid can be made to come in contact with the stone, an air pyelogram is most helpful (Fig. 5A and B). Air is preferred to a radio-opaque substance because it does not obscure the stone.

DETERMINATION OF CHEMICAL COMPOSITION OF STONES

Before attempting to dissolve a stone with Solution G it is, of course, necessary to know that one is dealing with a phosphatic stone. By a "phosphatic stone" is meant one composed of calcium phosphate with or without calcium carbonate or magnesium ammonium phosphate or both. In this clinic, to the present date, no attempt has been made to separate out the various subgroups of phosphatic stones. The composition can be determined by chemical analysis if a stone has been removed in the past, by circumstantial evidence¹ or by the x-ray appearance of the stone. This last method of analysis is most useful and has already been discussed¹; it will be taken up in more detail in another publication.⁶

CLINICAL RESULTS

Solution G has been used on approximately 20 patients. In this report 7 cases are presented. These have been selected to bring out certain points.

CASE REPORTS

CASE 1. (Long history of recurring bilateral calcium phosphate stones; etiology of first stones probably hypercalcaemia from immobilization and resulting atrophy of disuse; ingestion of milk and of calcium gluconate were added factors; stones on right dissolved with Solution G through nephrostomy tube.)

In 1928, W L (No 70740), at the age of 18, fractured his left femur and humerus. Because of nonunion he was immobilized in bed for 6 months and given large amounts

milk and the calcium gluconate. The fallacy of this procedure lay in the fact that there was no point in giving a high calcium intake since nonunion of fractures is due

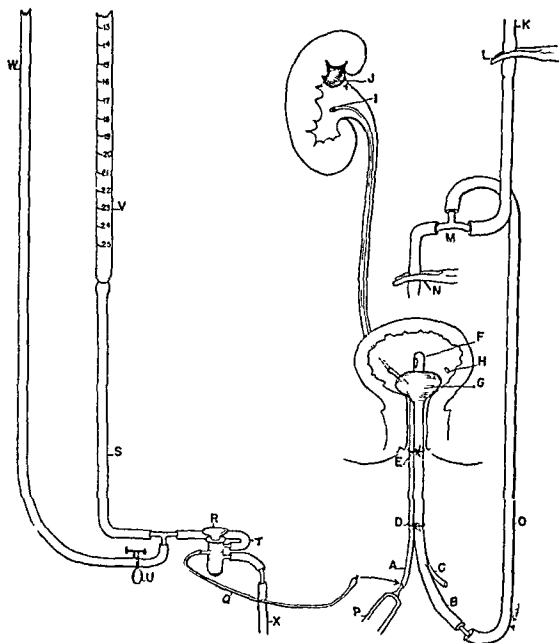


FIGURE 7. Apparatus If Dissolution Is to Be Carried Out through One Ureteral Catheter

A—ureteral catheter B—proximal end of Foley catheter C—tube through which balloon of Foley catheter is inflated D and E—sutures fixing ureteral catheter to Foley catheter F—distal end of Foley catheter G—balloon of Foley catheter H—ureteral orifice I—distal end of ureteral catheter J—stone K—tube leading to reservoir of fluid used in bladder irrigation L—forceps M—glass T tube N—forceps on tube leading to waste fluid bottle O—rubber tubing P—syringe through which Solution G is inserted Q—small-caliber tubing similar to ureteral catheter R—three way stopcock S—tube leading to burette T—rubber tubing U—clamp V—burette W—end of tube leading to Solution G X—tube leading to waste bottle

Since it is very irritating to void around a catheter it is necessary to have a bladder catheter as well as a ureteral catheter. A Foley catheter is used since it can be drawn tightly into the bladder neck and thus securely fixed. In this way a fixed object is furnished to which the ureteral catheter can be securely fixed. To irrigate the bladder one clamps the tube at N and opens the tube at L thus allowing fluid to go into the bladder. To empty the bladder one opens the tube at N and clamps the tube at L.

If the patient is to work the apparatus himself it is suggested that the apparatus at the left of the diagram be used instead of a syringe. The patient fills the burette to the desired level by opening the clamp U. To put fluid into the kidney tube the burette is connected through tubes S and T with the small tube Q by adjusting the three way stopcock R. To let fluid out of the kidney tube Q is connected with tube A by turning stopcock R. If a No. 10 Baidam tube is used for the ureteral catheter and for tube Q the dead space amounts to 3 cc. for 125 cm. of tubing.

of milk and calcium gluconate by mouth. Bilateral renal stones developed for which there was adequate reason. (Immobilization alone produces marked hypercalcaemia to this was added a very high calcium intake from the

to lack of formation of a callus, not to lack of calcification of a callus.) Left pyelolithotomy was performed but the stone is not analyzed. Nine years later the patient again entered the hospital with bilateral stones. A right

nephrolithotomy and a right nephrostomy were performed. When the present studies were started he had been wearing a nephrostomy tube for 4 years and some large stones

burning on urination. At the end of 10 days the stones were definitely smaller (Fig. 3B). Each week thereafter showed further improvement until the stones were entirely

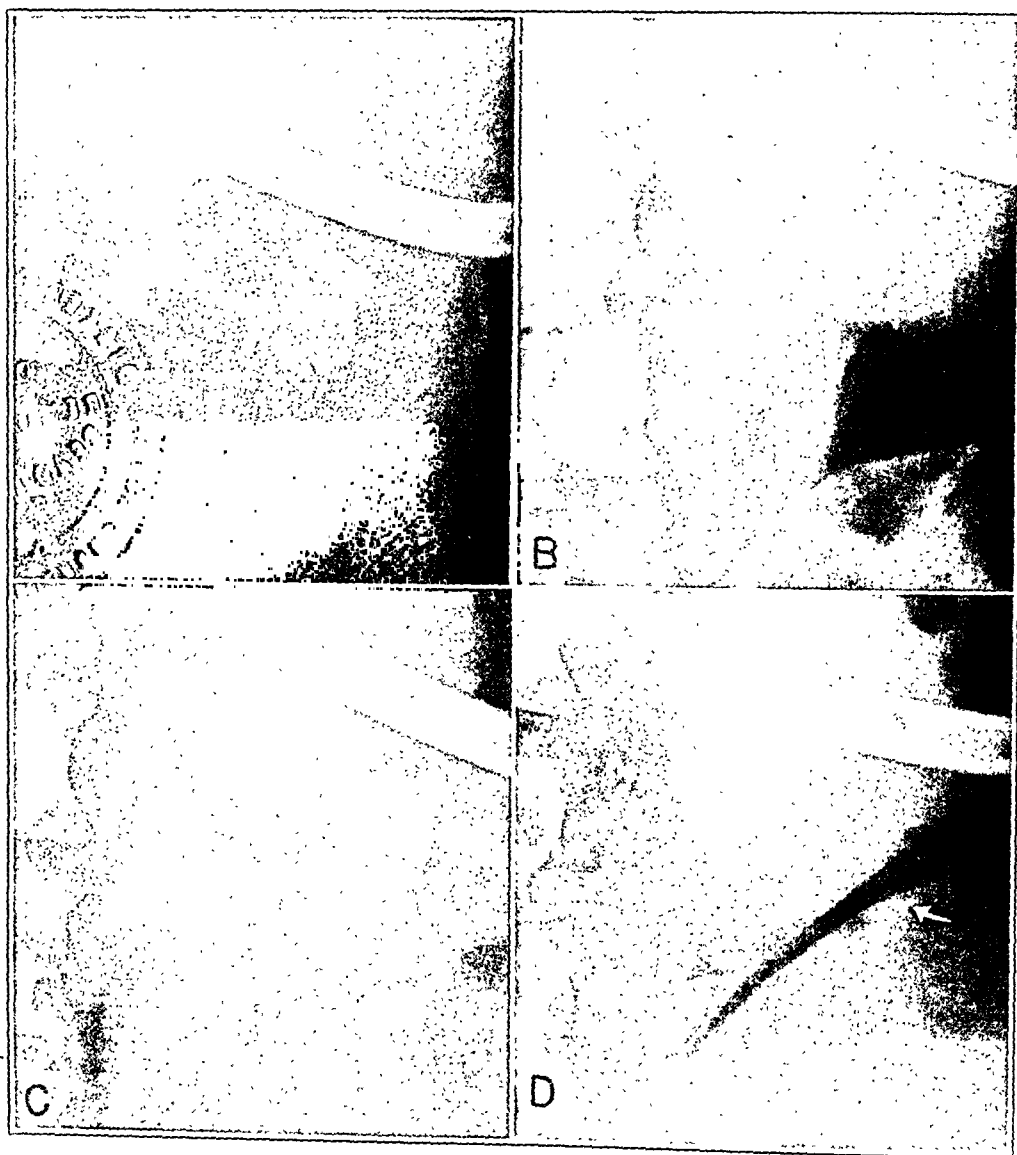


FIGURE 3. Roentgenograms in Case 1 before (A), during (B and C) and after (D) Dissolution of Stones.

In B, note that the small stone above the catheter has entirely disappeared and that the large stones below the catheter are much smaller; in D, note that the small residual shadow indicated by the arrow lies outside of the kidney pelvis, since air in the lower calyx does not extend to the shadow.

had formed in the right kidney (Fig. 3A). The serum calcium and phosphorus values were normal; the urine showed *Proteus vulgaris* on culture, which was probably the cause of the recurrent stone.

Solution G was introduced through the nephrostomy tube and allowed to pass out through the ureter, bladder and urethra. The solution ran approximately 9 hours a day between 7 a.m. and 7 p.m. The patient used in the neighborhood of 3000 cc. daily and did not experience

dissolved (Fig. 3C and 3D). The entire procedure took approximately 3 months; thereafter the nephrostomy tube was removed. During the time of irrigation the patient received 0.5 gm. of sulfathiazole three times daily. He was followed in the Out Patient Department for 1 year. At the end of that time *P. vulgaris* infection was no longer present; the urine contained some colon bacilli but was acid; a pyelogram showed no recurrence, and the patient resumed his work as a radio engineer.



FIGURE 4 Roentgenograms in Case 2 before (A), during (B) and after (C) Attempted Dissolution

Note that the stones which dissolved did so completely and that those that did not dissolve remained as they were because of lack of contact with the solution

CASE 2. (A man with a long history of recurring bilateral calcium phosphate stones; many operations; etiology of original stones obscure, possibly kinked ureters; more recent etiology infection with urea-splitting organisms; dissolution with Solution G through bilateral two-way nephrostomy tubes of those stones in contact with kidney pelvis.)

J. S. (No. 308796), in 1925, at the age of 17, developed stones in the left kidney, for which a left nephrolithotomy

CASE 3. (Attempted dissolution with Solution G through a nephrostomy tube of a stone not found at operation; difficulty with bladder irritability, which was finally overcome.)

J. D. (No. 236588), a 41-year-old man, entered with two stones in the left kidney pelvis and congenital absence of the right kidney. The serum calcium and phosphorus values were normal; the blood nonprotein nitrogen was slightly elevated. A left pyelolithotomy was performed

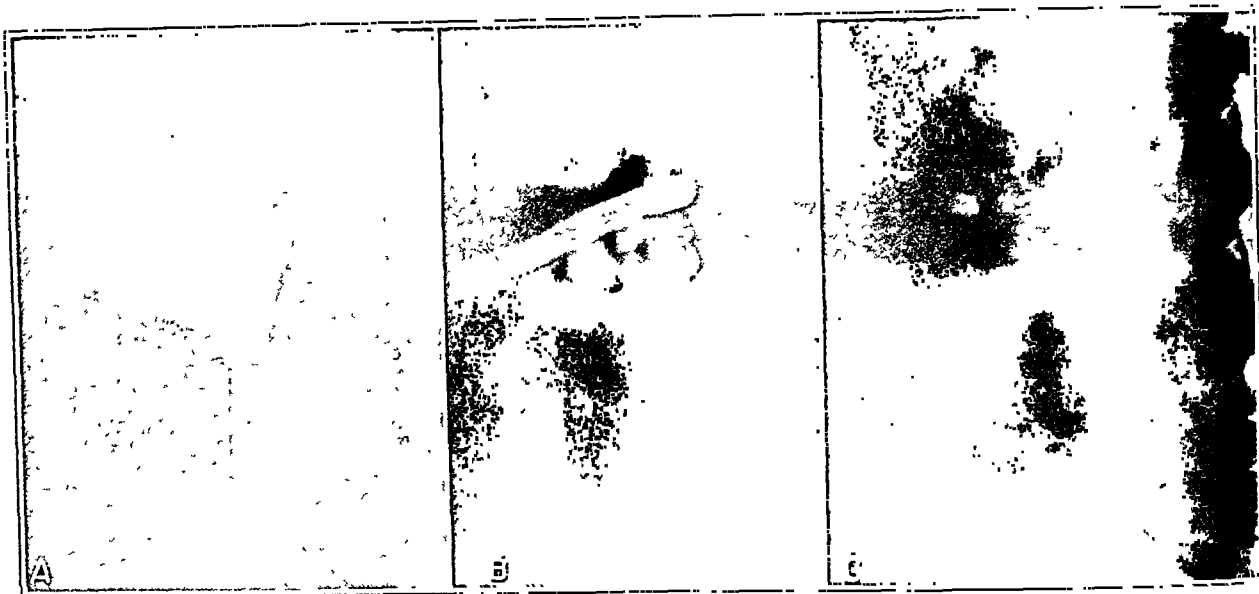


FIGURE 5. Further Roentgenograms in Case 2 to Show the Advantage of an Air Pyelogram (B) over a Pyelogram with Opaque Substance (A).

In B, note that the air does not extend down to the stone in the left lower quadrant of the picture but merely goes as far as the arrow; in C, which shows the stones after attempted dissolution, note that this stone remains undissolved.

was performed. In 1937, bilateral stones were found; in 1938 a right nephrolithotomy and a right nephrostomy were performed, and in 1939 a left nephrolithotomy and a left nephrostomy. The patient was referred to the Massachusetts General Hospital by Dr. Leo E. Gibson of Syracuse, New York.

The serum calcium and phosphorus levels were normal; the urine was constantly alkaline and contained *Escherichia coli* and a nonhemolytic streptococcus; the analysis of a stone that had been removed previously showed it to be pure calcium phosphate. Large bilateral stones were present (Fig. 4A). As the ureters were practically non-patent, it was impossible to use them for draining out the solution; consequently the nephrostomy tubes were connected to a modified Munro tidal-drainage system. This was without effect because of the large amount of dead space (see above). Therefore the simple nephrostomy tubes were replaced with two-way nephrostomy tubes and Solution G was allowed to run into one side and out the other (Fig. 1). The patient ran approximately 1500 cc. of the solution through each tube daily. Figure 4B and C shows the dissolution of the stones that were in contact with the kidney pelvis. Figure 5A and B shows the advantage of an air pyelogram for demonstrating the relation of the stones to the kidney pelvis. Unfortunately complete contact with the stones could not be made (Fig. 5B), so that the patient was discharged with a few fragments still remaining and sent back to work with nephrostomy tubes left in place.

but only one stone was found; accordingly a nephrostomy tube was left in place. An analysis of the removed stone showed it to be calcium phosphate. Two weeks after the operation Solution G was introduced into the pelvis through a nephrostomy tube at the rate of 40 to 60 drops per minute, but caused marked irritability when it reached the bladder. The patient was then cystoscoped and a soft-rubber ureteral catheter was passed to the kidney pelvis; Solution G was then introduced into this catheter and allowed to come out the nephrostomy tube. The stone was readily dissolved (Fig. 6A, B and C).

CASE 4. (Recurrent stones due to hyperparathyroidism; removal of parathyroid tumor, leaving residual stone in right kidney; stone stationary in size for a long period of time; then rapid growth following infection with *P. vulgaris* (*B. proteus*); dissolution of calcium phosphate cortex, with no change in calcium oxalate center, an outcome that could have been foreseen by x-ray studies.)

J. B. (No. 117408), a woman, had a right nephrolithotomy in 1938 at the age of 25; the stone was found to contain a large amount of phosphate and a moderate amount of oxalate. The serum calcium was high (12.1 mg. per 100 cc.), the serum phosphorus was low (2.7 mg. per 100 cc.), and a diagnosis of hyperparathyroidism was made. A parathyroid tumor was removed by Dr. Oliver Cope. There remained a small stone in the right kidney at the time of the parathyroid operation; this continued constant in size for the next 3 years. In June, 1941, however,

the patient was cystoscoped in an outside hospital and developed an infection with *P. vulgaris*. Thereafter the stone grew rapidly.

Although the center of the stone in x-ray films looked suspiciously like that of an oxalate stone, it was decided to attempt dissolution through a ureteral catheter. A No. 5 whistle-top catheter was introduced into the right kidney

during her second pregnancy she developed pyelitis. One year before admission she received a left nephrectomy because of calculus pyonephrosis. Six months later she had right renal colic and passed a stone. None of the stones had been analyzed. Four weeks prior to admission she developed complete anuria of 48 hours duration and attempts at ureteral catheterization were unsuccessful.

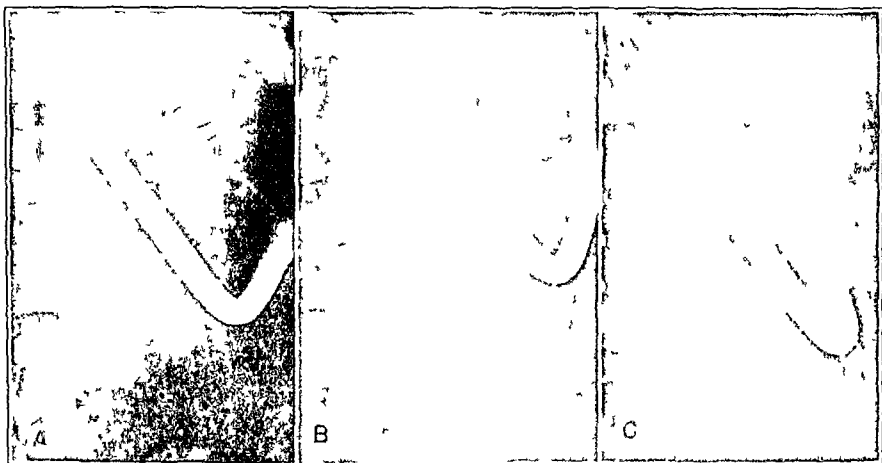


FIGURE 6 Koenigscopograms in Case 3 before (A) during (B) and after (C) Dissolution

Note that the stone is in contact with the pelvis is shown in B as a pyelogram

pelvis and left in for 24 hours during 14 of which 5 cc. of Solution G was introduced every 5 minutes. This catheter did not work very well however and the patient complained of pain accordingly it was withdrawn and a No. 10 Gareau catheter was passed. Five cc. of Solution G was injected into this catheter every 5 minutes for approximately 14 hours a day for 3 days. The Gareau catheter was then withdrawn and a No. 10 soft rubber catheter was introduced. The irrigation was continued for 6 more days. Figure 7A shows the stone before irrigation and Figure 7B after approximately 10 days of irrigation. It will be noted that the cortex of the stone was entirely dissolved. By more careful x-ray technique it was then demonstrated that the residual stone was calcium oxalate (Fig. 7D).

This case illustrates the importance of careful x-ray technique in order to rule out oxalate stones had it been known, as it could have been that the center of the stone was definitely oxalate the procedure would have not been attempted. As a matter of fact, the patient's symptoms were very much improved as a result of the procedure, and it is barely possible that the size of the stone was sufficiently reduced so that it may eventually be passed.

CASE 5 (Left kidney removed for calculus pyonephrosis remaining kidney totally blocked by right renal stone requiring emergency nephrostomy stones completely dissolved with Solution G bladder irritability overcome by closed urethral drainage.)

C.W. (No. 339467), a 25 year-old woman was perfectly well until 1½ years prior to admission. At that time,

A right nephrostomy was performed. The patient recovered from the operation and came under our control 3 weeks postoperatively. The wound was well healed the nephrostomy tube was draining well and she was passing nothing from the bladder. The blood calcium and phosphorus were within normal limits. The urine was alkaline and contained large amounts of pus. Culture showed *Staphylococcus aureus* and a nonhemolytic streptococcus. An air pyelogram revealed a stone 2 cm. in diameter in the right ureteropelvic junction and several small stones in the lower calyx (Fig. 8A). These had the characteristic x-ray appearance of calcium phosphate stones. An attempt was made to ascertain the patency of the ureter at this time but it was quite difficult to get liquid or air into the kidney pelvis. As salt solution was dripped into the nephrostomy tube it leaked out around the tubing. The lower calyx and infundibulum were apparently partially blocked by stone and mucus. By means of the Murphy drip apparatus we were finally able to run in Solution G very slowly. It was as if an exit for the fluid had to be dissolved out first. However, the lower calyx stone dissolved and the large pelvic stone began to crumble (Fig. 8B), later the larger stone completely disappeared (Fig. 8C). The patient had considerable bladder irritability once the solution began going through to the bladder. This complication was managed very easily by placing her on closed urethral drainage. Once she began to tolerate about 2000 cc. of fluid per day, the stone dissolved in about 10 days. Figure 8C is an air pyelogram showing that all the stones were dissolved. Figure 8D is a Neoskiodan pyelogram showing that although there

was still moderate hydronephrosis, the ureteropelvic junction and ureter became patent. The right nephrostomy

were hypercalcemia (serum calcium, 12.8 mg. per 100 cc.) and hypophosphatemia (serum inorganic phosphorus,

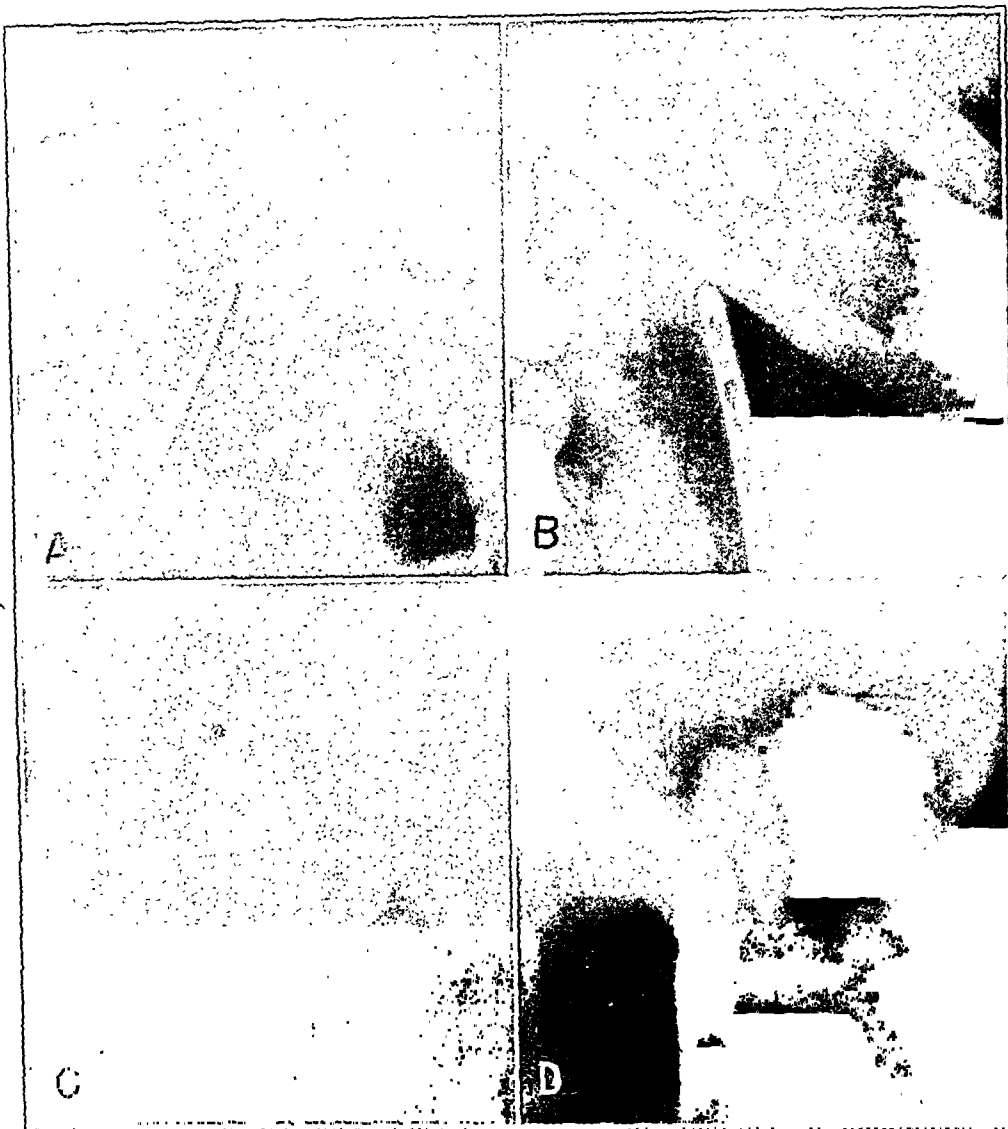


FIGURE 7. Roentgenograms in Case 4.

A—air pyelogram before dissolution; note the granular center and the less dense cortex of stone. B—stone after ten days of dissolution; note that the cortex has disappeared and that the remainder of stone has a granular appearance suggesting that it is an oxalate stone. C—larger magnification of A. D—a second roentgenogram of stone at same stage as B, with better x-ray technic to bring out the oxalate structure.

tube was removed, and the patient began to pass clear urine.

CASE 6. (A 15-year history of kidney stones, including right nephrotomy; a diagnosis of hyperparathyroidism made, and a parathyroid adenoma removed; bilateral stag-horn stones and pyelonephritis persisted; dissolution of stone on left through ureteral catheter.)

E. R. (No. 135241), a 49-year-old, married woman, first developed urinary symptoms at the age of 30. Three years later the late Dr. Arthur Chute removed three "alkaline stones" from the right kidney pelvis. Eleven years later she was referred to the clinic by Dr. Harvard H. Crabtree because of bilateral staghorn-kidney stones. Since there

2.3 mg. per 100 cc.), a diagnosis of hyperparathyroidism was made. A parathyroid adenoma was removed by Dr. Oliver Cope in June, 1938. (This patient was one of the two in the series of 68 patients with proved hyperparathyroidism who did not have an abnormally high calcium excretion in the urine when first seen.) She had an infection in the urine with the urea-splitting organism, *Staph. albus*, and was unable to acidify her urine. The phenolsulfonephthalein excretion was excellent, but the urine concentration failed to rise above a specific gravity of 1.012.

After the removal of the parathyroid adenoma the serum calcium and phosphorus values returned to normal, but otherwise there was no change in the patient's condition.

To be sure, the urinary calcium excretion fell from a normal level (about 90 mg. in 24 hours) to a low level (about 35 mg. in 24 hours). During the next 5 years she was followed in the Out Patient Department. The staghorn stones remained constant in size; the kidney function remained relatively unaltered. Small calculi were passed from time to time; these presumably were new stones due to the persistently alkaline urine.

On April 21, 1942, an indwelling soft-rubber catheter was introduced into the right kidney pelvis and dissolution of the stone with Solution G was started. The apparatus employed is shown in Figure 2. Two nurses were ob-

possible of course to introduce more fluid at a time; the largest amount used was 30 cc. The results are shown in Figure 9.

CASE 7. (Bilateral calcium phosphate and carbonate stones; etiology probably excessive intake of soda and cheese, left nephrectomy and right nephrotomy performed previously; attempt to dissolve stone in right kidney through indwelling catheter; cause of failure shown by x-ray study.)

R. W. (No. 354198), a 47-year-old, married woman, was admitted because of right renal stone. A left nephrec-

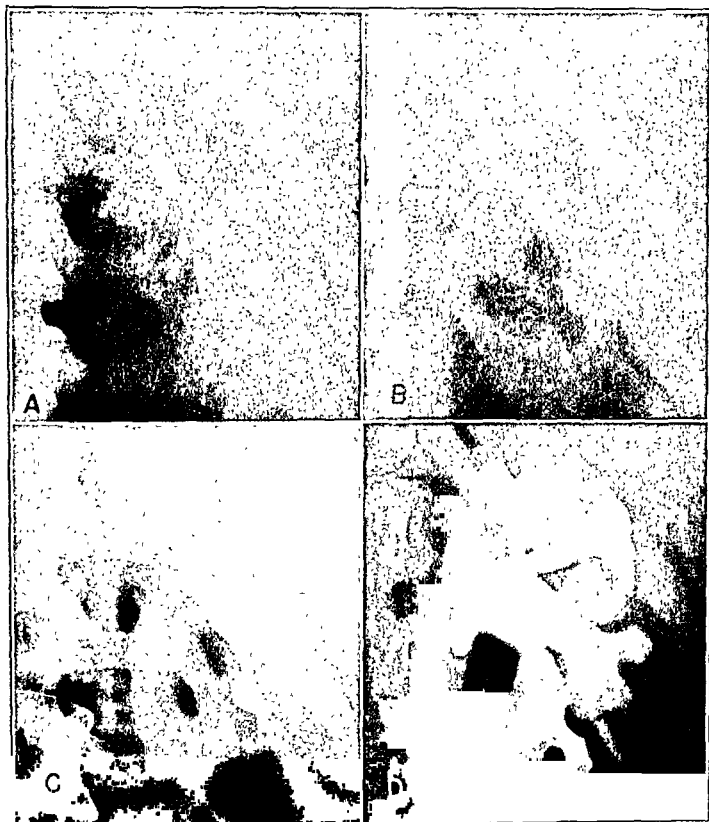


FIGURE 8. Roentgenograms in Case 5.

A—air pyelogram showing stones before dissolution. B—air pyelogram showing stone in lower calyx completely dissolved. C—air pyelogram showing all stones dissolved. D—pyelogram with opaque substance to compare with air pyelogram C.

tained, one for each of two 8-hour shifts; it was their duty to introduce Solution G by a syringe into the catheter every 4 to 10 minutes, to allow the solution to remain in the kidney 2 or 3 minutes, and finally to let it drain from the kidneys. As the stones dissolved away it was

tomy and right nephrotomy had been performed 1 year previously. The patient was for a long time in the habit of ingesting large amounts of soda and cheese. Stones removed at two previous operations contained large amounts of calcium phosphate and calcium carbonate.

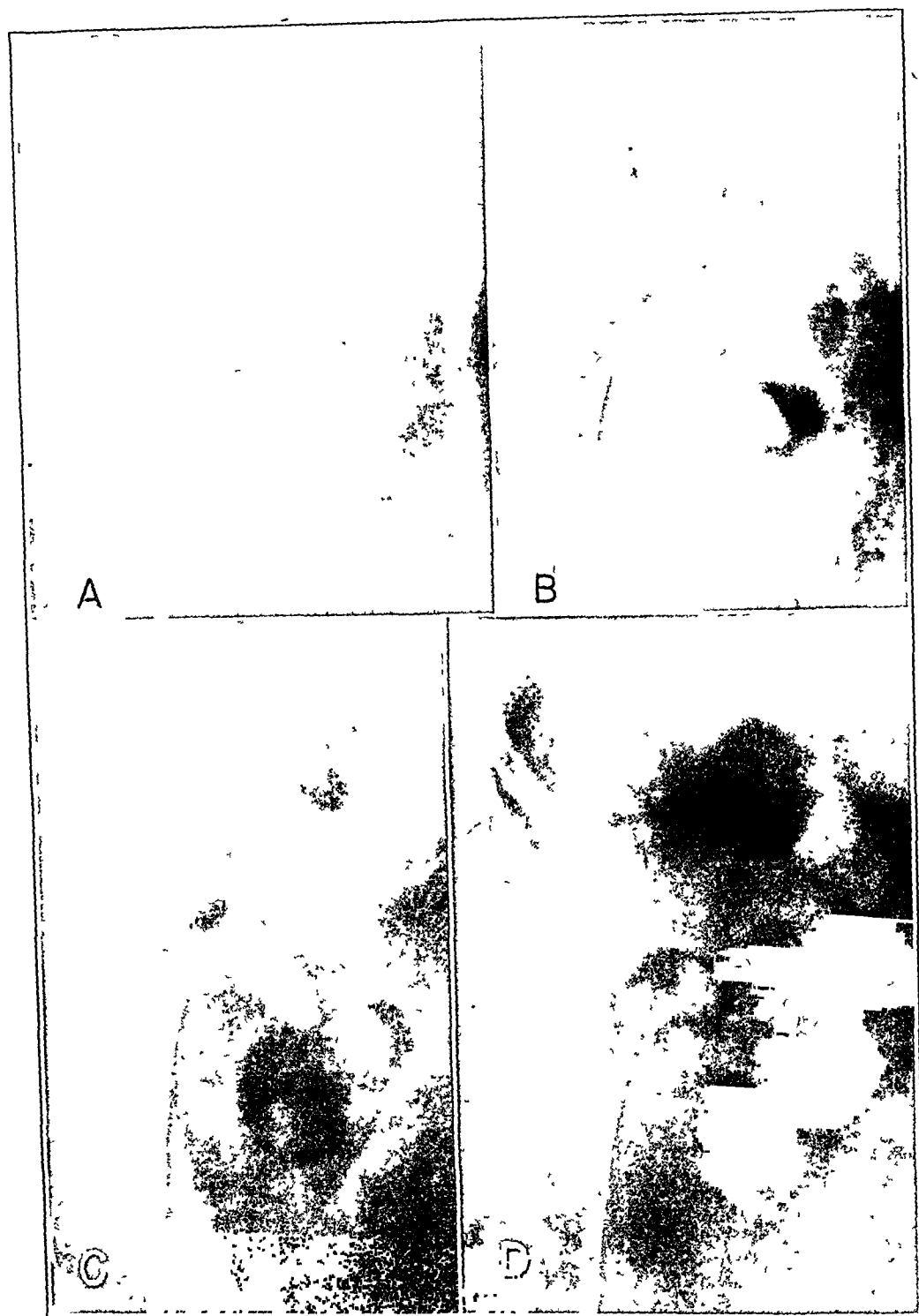


FIGURE 9. Roentgenograms in Case 6.

A—before irrigation, B, C and D—eleven, twenty and forty days, respectively, after onset of irrigation. Note that dissolution proceeded most rapidly in the calices. This was an unexpected result since it was feared that calyx stones would be the last to disappear.

The last stone removed from the right kidney was noted in addition to having a peculiar coating the external surface of which was not determined but which was thought to be clotted blood since it gave a strongly positive guaiac test. The serum calcium and phosphorus levels were within normal limits. A ureteral catheter was introduced into the right kidney pelvis and irrigations were carried out as in Case 5. Re-examination 6 days later showed a decrease in the size of the stone. Failure was undoubtedly

solution was prevented from coming in contact with the stone by a thin coating of unidentified material, possibly old blood clot.

The choice of apparatus depends on the individual case and the ingenuity of the operator. Ideally the hydrodynamics should be such that the pressure in the kidney is great enough to get

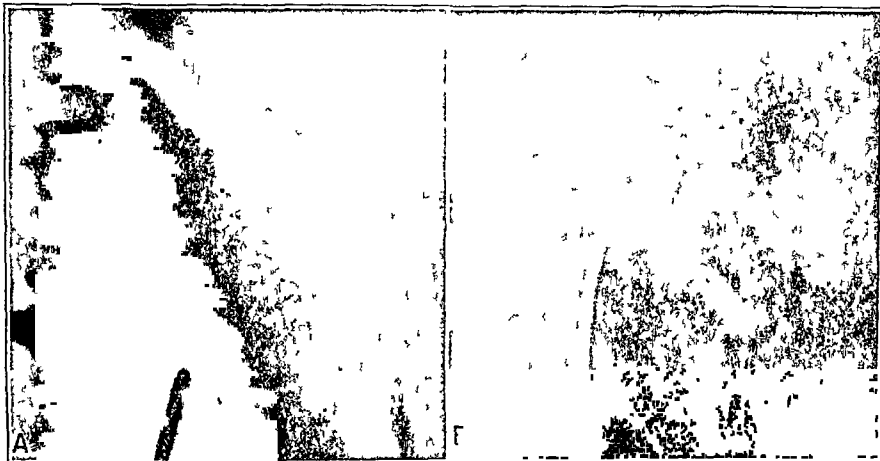


FIGURE 10 Roentgenograms in Case 7

A—stone before attempted dissolution B—pyelogram with opaque substance after failure to dissolve the stone. Note that the stone is coated with some substance that prevents the opaque material from coming in contact with it.

due to the capsule of organic material surrounding the stone which prevented its solution (Fig 10-A and B).

SUMMARY AND CONCLUSIONS

Citrate solutions rendered less irritable by the addition of magnesium are practical for the dissolution of urinary calculi composed of calcium phosphite, calcium carbonate or magnesium ammonium phosphate.*

Six selected cases are reported in which such a solution was used successfully for the partial or complete dissolution of stones, in 2 cases the solution was introduced through ureteral catheters, in the remaining 4 through nephrostomy tubes.

One case is reported in which attempted dissolution of a large stone was without success because the

the solution around the stone, but sufficiently intermittent so that a pyelonephritis is not produced by a constant back pressure.

For determining whether a stone is in contact with the kidney pelvis and for following the course of dissolution, the advantages of an air pyelogram are stressed.

The importance of the roentgenogram in determining whether the stone is of the soluble variety is pointed out, a case is cited in which the centre of the stone was calcium oxalate and hence indissoluble, a finding that could have been determined by suitable x-ray technique.

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*The solubility of Sodium Citrate is probably increased by the fact that a pH is lower than that of the urine reaches. It may be that a solution with a pH of 4.5 would be long run better. What we could do is to decrease the speed of solution and might only the likelihood of solubility.

The form of such a solution (Sodium Citrate) is as follows:
 Citric acid 32.35 gm
 Sodium carbonate (anhydrous) 8.84 gm
 Magnesium oxide 3.84 gm
 Water qs ad 100.0 cc

As judged by solubility tests of calcium citrate solution on M.W.I. to in two cases it was that sodium citrate solution.

EPIDEMIOLOGIC ASPECTS OF ANTHRAX IN MASSACHUSETTS*

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TIMES of war bring a host of new problems and an intensification of old ones in medicine as well as in many other fields. Anthrax, known since antiquity as an agricultural disease, presents in these days of stress an increased potential industrial hazard, for, in the anxiety to get leather, hides are obtained wherever available. Many are imported from countries where anthrax is still a common disease. In this connection it may be mentioned that in 1938 in Bulgaria, with a population of only 6,500,000, between 800 and 1000 human cases and 2716 animal cases of anthrax occurred.¹ At present, many hides in the United States come from India and China, countries where anthrax is prevalent.

With the wartime influx of potentially infected hides, the epidemiologic control of anthrax presents a greater problem than ever. Public-health supervision of importation and transportation is imperative. Smyth,² in a twenty-year survey in the United States (1919-1938), reported an incidence of 1683 cases. In Massachusetts, in the seven and a half years, from January, 1935 to July, 1942, 43 cases have been reported. That the incidence has not been greater is merely fortuitous, and it may rise rapidly in the near future. Anthrax spores are extremely difficult to kill; and to this day no commercially practicable method of destroying spores in hides has been discovered, since all known methods are complicated and expensive. Although this was the first disease entity to be proved by Koch's postulates,³ no significant advances in its control have been made in the last twenty years.

Man and all animals, especially the herbivora, are susceptible to infection with *Bacillus anthracis*.⁴ Normally the organism is indigenous only in certain areas, called "anthrax districts," and in such places animals are sporadically infected during some period of the year, usually in the summer. Isolated cases, however, may occur at any time. Anthrax being primarily a disease of animals, it frequently happens that agricultural workers become infected. It is also apparent that workers who deal with any by-product of an animal may contract the disease; included among such workers are those who deal with hides, wool, bristles, and hair. Longshoremen, truckmen and a group of miscellaneous workers, such as brushmakers, butchers, gluemakers and upholsterers, may also be

infected. In animals, anthrax is caused by ingestion and any medium that spreads the bacillus may cause an outbreak. In man the spore usually enters through a break in the skin, forming the so-called "malignant pustule." It may, however, be ingested and, in some cases, as in woolworkers, may be inhaled, giving rise to the pulmonary form of the disease.

In 1940, the United States Bureau of Animal Industry⁵ decided that the possibility of the spread of anthrax to domestic animals from imported fomites was relatively slight and, with certain specified exceptions, lifted its restrictions on the importing of hides. It is important to recognize that this bureau is interested primarily in the control of animal disease and not in the control of human disease. Theoretically, consular inspection at the point of origin of foreign hides is maintained. In normal times this inspection is subject to error, and under the stress of war it can at best be only perfunctory. Dry hides that are imported are subject only to a treatment (with bifluoride or silicofluoride) known to be effective against rinderpest and hoof-and-mouth disease. The effect of this treatment on anthrax spores is unknown and may be presumed to be nonefficacious, since infections have occurred from hides that have been treated in this manner.⁶

There have been 4 deaths and 39 recoveries in the 43 cases that occurred in Massachusetts from 1935 to 1942. The incidence by years is shown in Table 1. An average of 5.7 cases a year have

TABLE 1. *Anthrax Morbidity and Mortality.*

YEAR	NO. OF CASES	NO. OF DEATHS	MORTALITY %
1935	3	0	0
1936	9	1	11
1937	6	0	0
1938	5	1	20
1939	2	0	0
1940	9	0	0
1941	6	1	16
1942 (to July 1)	3	1	33
Totals	43	4	9.3

occurred. The lowest incidence was in 1939, with only 2 cases, which was followed by a sharp increase to 9 in 1940. In 1941 there was a decline to 6 cases, and in 1942 up to the present writing (July 1), 3 cases have been reported.

The occupations involved are shown in Table 2. Massachusetts has a large leather industry, and this is reflected in the fact that tannery workers

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account for 32 cases comprising almost three quarters of the total. The majority of men infected worked either in beam houses or in storehouses

TABLE 2. *Incidence of Anthrax according to Occupation*

OCCUPATION	NO OF CASES	NO OF DEATHS	MORTALITY
			%
Tannery workers	32	1	3
Truckmen and longshoremen	4	2	50
Hair and bristle workers	3	1	33
Agricultural workers	2	0	0
Woolsorter	1	0	0
Miscellaneous (welder)	1	0	0

No authentic case could be traced to infection from finished leather. The next largest group, truckmen and longshoremen (4 cases), were all engaged in the transportation of imported hides. One more case could be traced to hides, as a welder was infected from his equipment, which had become contaminated by unfinished leather. Hence in all, a total of 37 out of 43 cases, or 87 per cent occurred in connection with hides. In not a single case could the infection be definitely traced to domestic skins. In 1 case it was thought to be due to domestic sheepskins, but the tannery concerned handled large amounts of imported hides, and the chance of cross infection was considerable. In an overwhelming majority of cases goatskins coming from India or China were the responsible agents. Four tanneries account for the major amount of imports, and in them occurred 27 cases or 63 per cent.

Three cases occurred among workers in hair and bristles, one of whom developed the only case of internal anthrax in this series. This man had both cutaneous and intestinal lesions and died. Certain by-products of animals, especially hair and bristles, are still subject to sterilization; hence, although outbreaks do occur, they are relatively rare. Two cases occurred in men engaged in domestic agricultural pursuits. One was a veterinarian who autopsied the carcasses of several cattle that had died of anthrax; the other was the owner of a milk farm where the animals became infected by eating anthrax-infected horsemeat. One case occurred in a woolsorter who scratched himself and developed cutaneous anthrax.

Although only 4 truckmen and longshoremen were infected with anthrax, 2 of them died. This high mortality, although not significant because of the small number of cases, is directly attributable to the lack of knowledge of the hazard of the disease on the part of the transportation companies and their employees. It was, therefore, not recog-

nized until late, with a consequent delay in therapy. Among tannery workers, where anthrax is suspected in any cutaneous infection, diagnosis and treatment are prompt, with a consequent decrease in morbidity and mortality. In the 32 cases that occurred in this group, there was only 1 fatality.⁷

SUMMARY AND CONCLUSIONS

It appears to be impossible to destroy anthrax at its source. Sporadic cases of native origin will always occur. It is extremely difficult to disinfect hides and skins. The anthrax spore undoubtedly survives the first two or three processes in tanning—that is, washing, fleshing and liming—but probably cannot survive the entire process. No significant improvement in the method of killing anthrax spores has been evolved in the last twenty years; and even if it were possible to disinfect hides and skins, it is doubtful whether this would be warranted, especially at the present time. Therefore the method of control must be chiefly one of education and sanitary precaution until the hides have passed through the tanning process. The more severe cases and the most frequent deaths have occurred in truckmen and longshoremen, who are not aware of the possibilities of this infection and who neglect to report for treatment early. The prompt diagnosis and treatment in tannery workers seem in large measure responsible for the lessened mortality and morbidity among them. Physicians treating any cutaneous infection in a tannery worker or truckman should bear in mind the possibility of anthrax and should culture material from the lesion. In order to keep this disease in check effectively, an educational program must be directed toward truckmen, tannery workers, longshoremen and all others who handle imported hides, from their arrival in this country to their conversion into finished leather.

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MONTESQUIEU: A BIOLOGIST OF THE EIGHTEENTH CENTURY

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NEW YORK CITY

IN HIS profound study of the development of modern medicine, Shryock,¹ speaking of the physicians of the eighteenth century, points out that Voltaire, the great lay critic, held saner views on medicine than did most of his professional compatriots. This fact constitutes perhaps one of the most striking features of the beginning of this remarkable century. The men who were guided by reason only, the "philosophers," did not have to overcome the bookish prejudices that surrounded stagnant medicine like a Chinese wall. For although at this time medicine was greatly harmed by Molière's biting mockery, it continued nonetheless to be merely a study and an interpretation of classical texts—as one might say, *more theologico*.

Medicine progressed with slower steps than did the other sciences. Where, indeed, are the physicians of this period who can be ranked with Linné, Buffon, Volta and Galvani?

Along with Voltaire, Shryock should have been able to quote Charles Louis de Secondat, Baron de la Brède et de Montesquieu (1689-1755), who throughout his work never ceased taking a great interest in medicine and physicians. The author of *L'Esprit des lois*² and *Lettres persanes*³ merits a place in medical history. I am sorry to state that I could find no mention of him in classical treatises.

I shall aim to fill the gap concerning a man who is considered rightly as one of the most humane and most eminent writers of French literature and whom physicians can be proud to count as one of theirs.

How did this man treat the field of medicine?

The Academy of Bordeaux, of which Montesquieu had been a member since 1716, had chosen as the prize subject "The function of the renal glands or atrabiliary capsules" (we should say, "The physiology of the suprarenal glands"). On August 25, 1718, Montesquieu announced in a speech before this esteemed society that the prize of the Academy could not be awarded to any competitor. In a clear statement, which showed his deep knowledge, he gave the reasons for this decision. But his interest was attracted by an abstract that had been submitted.

Another [he said] who fortunately defined the difference between conglobated and conglomerated glands considered the atrabiliary capsules as a conglobated one. He believes that they are only a continuity of vessels in which the blood like in channels is subtilized. . . .

In these glands, and in every conglobated gland, there is no excretory duct, because there is no matter to separate liquids, but only to subtilize them. This system, not without some appearance of truth which is captivating at first, had attracted the attention of the society. But the author could not maintain his thesis.

And while the author of this luminous hypothesis still remains unknown, Montesquieu at least deserves credit for having transmitted it to our admiration. We know today how true this thesis was! But it was a long time before our knowledge was acquired. Anatomists like Gegenbaur† rejected even in 1903, about two centuries after the meeting of the Academy of Bordeaux, the idea of glands in which the excretory duct is supplied by blood vessels. Can we, therefore, upbraid Montesquieu for having doubts about this thesis, which seemed unlikely even to unquestionable masters of anatomy in our time? The members of the Academy assured themselves of the difficulties of the subject. They ordered experiments and dissections to be made so that they could "see with their own eyes," and thus they understood why the solution of the thesis had not been found.

"Chance will perhaps do some day," Montesquieu added, "what every effort could not do." And he closed his speech with these words which investigators can use as a motto:

Those who make their profession the seeking of truth are no less subject to the caprice of fortune than are others. What today costs so much needless toil can perhaps not withstand the first considerations of a happier author. Archimedes found while taking a delightful bath the solution of the famous problem which he had missed a thousand times while reflecting deeply. Truth seems sometimes to run before the seeker. Frequently there is no interval between desire, hope and enjoyment. Poets tell us that Pallas went out of Jupiter's head without pain, to make us conscious that the products of the spirit are not always tiresome.

The "Observations on Biology," which Montesquieu read on November 20, 1721, merits our admiration because it demonstrates the probity and the scientific spirit of the author. What a diversity of related facts! The pigmentation of insects was studied microscopically, the parasitism of mistletoe was examined carefully, the abdominal circulation

†Gegenbaur† writes: "We used to range thyroid and thymus along with some other glands, which have a 'mysterious' physiology, as 'blood glands.' Some authors consider them as glandular organs in which the excretory duct is replaced by blood vessels. The excretory duct, however, constitutes an essential part of a gland, which cannot be supplied by blood vessels. It is by no means evident how blood vessels physiologically can supply a part of an organ or how these organs secrete something that goes into the blood."

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of the frog was exposed with great precision. Finally, many problems of vegetal physiology, as well as studies on the foramen ovale and Botrillos duct, are noteworthy. The last chapter of these observations concerns experimental researches on the nutritional value of some vegetables.

One imagines [he wrote] that only wheat has food value for the human being and one considers that the other plants are merely of medical use. Physicians find them emollient, diuretic, desiccative or astringent. They treat all like manna, which nourished the Jews and which they use as a purgative. They give them an infinity of qualities which they do not have and nobody thinks of the nutritional virtue which they have. Wheat, barley, rye, like other plants, have years which are very favorable to them. There are years when the scarcity of corn does not constitute the unique misery which causes sorrow to people. Their bad quality is still more cruel. In these years calamitous for the poor and a thousand times more calamitous for the rich in a religious nation, we are able to supply the deficiency of corn. We have under our feet in every wood a thousand resources, against dearth and for that we should praise instead of curse Providence if we would know all his benefits. And therefore we intend to examine plants, herbs and an infinite number of things which apparently have no nutritional virtues. Animals which have some resemblance to human beings can well be used for this purpose. We have begun some of these experiments with great success. The shortness of time does not permit us to quote them here.

What a pity that this report did not come down to posterity! Montesquieu told us that his research work was the fruit of leisure hours in the country. For the author of *L'Esprit des lois* considered that leisure must be profitable to mankind. "Those who are living in a community," he wrote, "have to fulfill a duty, we have to account for every diversion."

Thus the lucid Montesquieu could only condemn and distrust the medicine of his time. He thought that the human spirit was stifled in the heap of theses of an obsolete and absurd "science." He held in abhorrence "this dreadful army of glossators and compilers who are as weak through the dullness of their advice as they are strong through their tremendous numbers." "And that is not all," he continued, "these foreign [Roman] laws have introduced formalities so excessive as to be a disgrace to human reason." And, again, "It would be very difficult to decide whether the pedantry has been more harmful in jurisprudence or in medicine, whether it has played more mischief under the cloak of a lawyer or the broad brim of a physician, and whether the one has ruined more people than the other has killed."

In a letter from a country physician to a physician of Paris, the mockery of Montesquieu reaches a peak.

There was once in our town a sick person who had no sleep for thirty five days. His physician ordered him opium but he could not make up his mind to take it, and when he had the cup in his hand he was less inclined than ever. At last he said to his physician, "Sir, give me only till tomorrow. I know a man, who although he does not practice medicine, has in his house an immense number of cures for insomnia. Let me send for him, and if I do not sleep tonight, I promise to return to you." The physician being dismissed, the sick man had his curtains closed, and said to his page, "Go to M. Anis and ask him to come to me." When M. Anis came, the patient said to him,

"My dear sir, I am dying. I can't sleep. Have you not in your shop the *Connaissance du globe* or some other book of devotion written by an R. P. I which you have not been able to sell, for long kept remedies are often the best?" "Sir," replied the bookseller, "I have the *Holy Court of Father Causin*, in six volumes at your service. I will send it to you and I hope you will be the better for it. If you would prefer the works of the Reverend Father Rodrigo a Spanish Jesuit you need not want them. But believe me you had better stick to Father Causin. I trust, with the help of God, that a single sentence of Father Causin's will do you more good than a whole page of the *Connaissance du globe*." With that M. Anis left and went to his shop to get the remedy. The *Holy Court* arrived and the dust having been shaken off of it the son of the sick man a schoolboy began to read it. He was the first to feel its effects. At the second page his utterance began to be almost inarticulate and already the whole company was growing drowsy. In a moment every body was snoring except the sick man, who after having stood it a good while was at last overcome too.

The physician arrived early next morning. "Well he said his mottoes been taken?" Nobody answered him. The sick man's wife daughter and little boy radiant with joy, showed him Father Causin. He asked what it was. They answered, "Long life to Father Causin, we must send him to be bound. Who would have said it who would have thought it? It is a miracle. Look sir look here is Father Causin. It is this book which has given my father sleep. And thereupon they explained the matter to him as it happened.

The physician was a skillful man versed in the mysteries of the Cabala and in the power of words and spirits. He was much struck and after deep thought resolved to change his practice entirely. Here is indeed a notable fact said he. It is a new experience and I must experiment further. And why should a spirit not be able to transmit to its work the same qualities which itself possesses? Do we not see it every day? At least it is well worth the trying. I am tired of the apothecaries their syrups the juleps and all their galeonic drugs destroy the health and the lives of their patients. Let us change the methods and try the power of the spirits. With this idea he drafted a new system of pharmacy, as you will see by the description which I am about to give you of the principal remedies which he employed.

A LIGHT PURGATIVE

Take three leaves of Aristotle's *Logic* in Greek, two leaves of a treatise on scholastic theology, the keener the better, as for example that of the subtle Scotus four of Paracelsus one of Avicenna six of Averroes

three of Porphyry; as many of Plotinus; and as many of Iamblichus. Infuse the whole for twenty-four hours, and take four doses a day.

This is only one example of a long list of prescriptions of the same kind. It would be too tedious to quote them. His favorite authors, I suppose, are not used as an ingredient of any decoction, even as an emollient one!

~ * *

"We have enough physicians. We now need medicine," he exclaimed once. He knew that there was no parallelism between medicine and the other sciences concerning progress.

Books of medicine [he wrote to express the same idea], those monuments of the frailty of nature and of the power of art, which, when they treat even of the slightest disorders, make us tremble by bringing the idea of death home to us; but which, when they discuss the power of remedies, make us feel as secure as if we were immortal.

Near these are the books of anatomy which do not so much contain descriptions of the parts of the human body as the barbarous names which have been given them — neither likely to cure the patient of his disease nor the physician of his ignorance.

People would perhaps blame Montesquieu for entertaining prejudices concerning medicine and physicians. Some may believe that his critical spirit prompted him to laugh at everybody and everything. But, satirizing with brilliant audacity the follies of his time, he could not avoid taunting our profession.

In a letter written May 5, 1753, to his good friend, Father de Guasco,* he expressed great admiration for Van Swieten, who was called by Maria Theresa from the Netherlands to Vienna to reorganize medical education. This famous physician, who was also chairman of the board of censors of Austria, authorized that Montesquieu's

book *L'Esprit des lois* could be sold in the Austrian Empire. Montesquieu held in devoted affection his physician Chevalier Louis de Jaucourt, who was a collaborator in the *Encyclopedia* for the section of physiology and pathology.

Montesquieu, who with his brilliant intelligence inquired into charges against the institutions and customs of his time, had to speak in his list of accusations of medicine and physicians. In the Academy he showed which way medicine had to take if the physicians would avoid irreverence and ridicule.

Antoine Portal, professor of anatomy of the Collège de France and the Jardin du Roy, gave this praise of Montesquieu: "We cannot say without admiration that, if Montesquieu had applied himself to anatomy, the progress of this science would have been as important as that of the ethical sciences under his guidance."

The mockery of *Persian Letters* is worthy of Molière's plays. Montesquieu's probity would not have permitted an unjust attack. He was a sincere moralist. "I never saw weeping without being moved with pity. I have committed many blunders during my life but never a malicious act."

He once wrote this sentence, which should win him immortality: "If I should know something useful to my fatherland but detrimental to Europe and mankind, I should consider it a crime." But Montesquieu knew that by remaining passionately a Frenchman he could be a good citizen of the earth.

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*Who was also a friend of Lord Chesterfield

MEDICAL PROGRESS

OBSTETRICS: MEDICAL ASPECTS

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AMONG the medical aspects of obstetrics, the toxemias of pregnancy continue to hold the center of interest because of their general influence on the occurrence of hypertension and albuminuria in women. Various attitudes regarding the relation of these conditions in pregnancy to the general problems of vascular and renal disease have led, in the past, to many differences of opinion. Contradictory results were often found, not only in clinical studies of these diseases but also in the physiologic studies made on patients. To promote a better understanding of the clinical syndrome known as the toxemias of pregnancy, a universal classification of diagnosis appeared most desirable. Through the American Committee on Maternal Welfare such a classification was presented in 1940¹; it has been accepted, and is now being used by all the large obstetric clinics of this country. This has been a landmark in the advance of the study of this disease for, although the classification may have certain weaknesses, it offers an opportunity to provide an accurate diagnosis in terms that are familiar to all. To emphasize the importance of this classification, it is given below.

GROUP A. Diseases not peculiar to pregnancy.

1. Hypertensive disease (hypertensive cardiovascular disease).
 - a. Benign (essential).
 - b. Malignant.
2. Renal disease.
 - a. Chronic vascular nephritis or nephrosclerosis.
 - b. Glomerulonephritis.
 - c. Nephrosis.
 - d. Other renal disease (such as pyelonephritis).

GROUP B. Disease dependent on, or peculiar to, pregnancy.

1. Pre-eclampsia.
 - a. Mild.
 - b. Severe.
2. Eclampsia.
 - a. Convulsive.
 - b. Nonconvulsive (that is, with coma and post-mortem findings typical of eclampsia).

It is evident from this classification that the obstetrician is aware of the role that vascular disease and renal disease play as a background for the toxemias of pregnancy (Group A). He also knows that the majority of patients with this syndrome develop, for the first time during pregnancy, varying degrees of albuminuria and hypertension (Group B). Finally, it is also realized that occasional cases may require a combined diagnosis from Group A and Group B, that is, pre-eclampsia superimposed on pre-existing vascular or renal disease.

With such a classification in universal use, and with the pooling of the experience from many clinics, it is possible to offer a solution of some of the problems that are bothersome during pregnancy, as well as to evaluate the renal and vascular sequelae that follow a toxemic pregnancy. Some of the more pertinent medical questions might be the following:

Which individuals with established vascular or renal disease should be allowed to continue their pregnancies?

If such patients are allowed to continue their pregnancies, what is the maternal and fetal risk involved?

What would be the effect of pregnancy on the course of the previously established vascular or renal disease of the mother?

What are the sequelae of the so-called "specific toxemia of pregnancy" on the vascular or renal system of previous normal persons?

Although many observations have been made to determine the ante-partum and post-partum status of the vascular and renal systems of patients in the different groups, no uniform answers to these questions have been given by the clinicians.

Albuminuria being a constant finding in the toxemias of pregnancy, attention was first focused on the kidney as the organ most profoundly affected by the course of this disease. However, it was soon found that marked changes could be observed in the liver, brain and other vital organs. Moreover, the degree of these changes was extremely variable. It has been emphasized that they are best explained by damage to the vascular system, particularly the small arterioles. Spasm of the smaller vessels oc-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29031

PRESENTATION OF CASE

A thirty-nine-year-old man came to the hospital because of recurrent fractures of the right humerus.

Twelve years before entry the patient first broke his right humerus, while engaging in an arm-wrestling game. At this time the arm was immobilized in a sling for six weeks. Six years later, while hammering with a 5-pound mallet, the fracture recurred. After six weeks of immobilization in a sling, union was apparently firm. One and a half years before admission the humerus was again fractured when the patient attempted to raise himself through a trap door. The treatment was similar to and as successful as that previously employed. Two days before entry, following what seemed to be slight trauma, the fracture recurred. The patient believed that though the same bone was involved each time, the fractures did not occur at the same level.

The family and past histories were noncontributory. He had never fractured any other bone.

Physical examination disclosed a well-developed and well-nourished man in no obvious distress. The examination of the lungs, heart and abdomen was negative. There apparently were false motion and soft-tissue swelling at the junction of the middle and lower thirds of the shaft of the right humerus, with slight anterior displacement of the distal fragment. The bones did not seem massive, and the skull was not enlarged. There was some pigmentation on the back.

The blood pressure was 112 systolic, 66 diastolic. The temperature was 97.6°F., the pulse 60, and the respirations 20.

Examination of the urine revealed a specific gravity of 1.018 and a neutral reaction; the sediment contained only a great deal of amorphous material. The blood Hinton test was negative. The blood calcium was 11.6 mg., the phosphorus 4.48 mg. and the phosphatase 17.1 Bodansky units per 100 cc.

An x-ray film demonstrated gross abnormalities of the right humerus in the upper three fourths (Fig. 1). There were large irregular areas of rarefaction along both the cortical and medullary

portions, giving the bone a cystic appearance. There was expansion of the shaft in its middle third, whereas in the upper third the shaft was narrow and increased in density, with coarse tra-

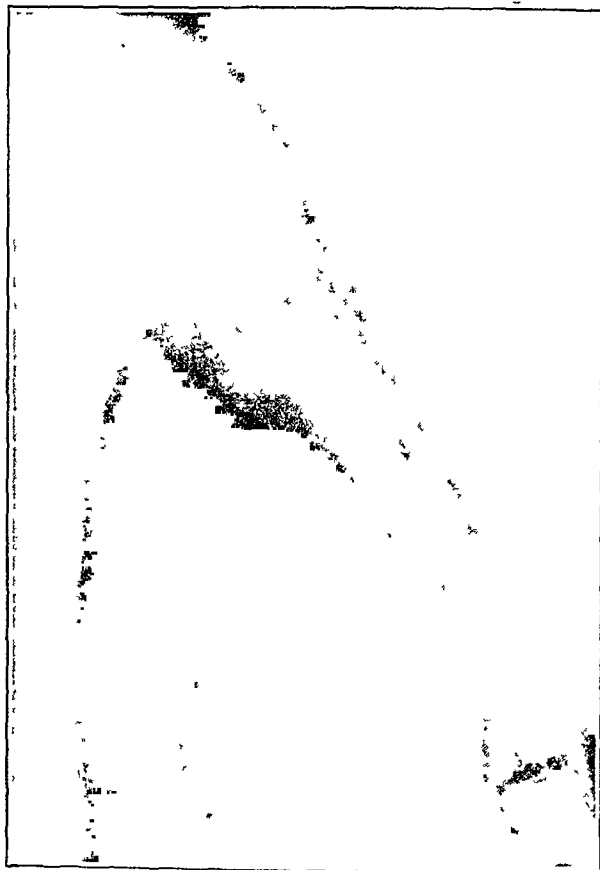


FIGURE 1.

beculations. There was a pathologic fracture at the junction of the middle and lower thirds, with slight anterior displacement of the distal fragments. Several cyst-like areas were seen in the lower part of the bone and in the upper shaft of the radius. The uninvolved portions of the bone were not definitely decalcified.

On the third day after admission, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FULLER ALBRIGHT: I cannot remember ever getting one of these cases right. If I do not get this one right I will be surprised and chagrined.

I see very few problems here. "There was some pigmentation on the back." We should like to know what kind of pigmentation. No, we do not really want to know, because it is not that! By "that" I mean osteitis fibrosa disseminata, which is often accompanied by areas of café-au-lait pigmentation. But since pigmentation was mentioned, they might have told us what kind it was.

The phosphatase is high for an adult. Even for a fracture it is high.

This is really an x-ray problem, and all we have to do is look at the x-ray films and make a diagnosis.

DR. GEORGE W. HOLMES: All these films were taken on the same day. They show a cystic lesion that ends abruptly. There is normal bone in the lower half of the humerus, and pathologic bone above it. It is an extensive lesion, with marked increase in the trabeculation of the entire upper end of the bone. There may be slight periosteal proliferation. Do you attach any importance to the fact that it apparently involved the end of the bone?

DR. ALBRIGHT: No. It can do this in either osteitis fibrosa disseminata or in osteitis deformans (Paget's disease).

DR. HOLMES: In Paget's disease the lesion always goes to the end of the bone. I am not saying it is Paget's disease.

DR. ALBRIGHT: But I have seen at least one good case of Paget's disease that did not go to the end.

DR. HOLMES: That may have been the exception that proves the rule.

DR. JOSEPH AUB: Did you say this was Paget's disease, Dr. Albright?

DR. ALBRIGHT: No, but I am going to.

The pathologic process involves not only the humerus but also, according to the record, the radius on the same side. That makes us think of one disease in differential diagnosis, namely osteitis fibrosa disseminata. We do not have to think of any other. I should like to see x-ray films of the hand of the same side. If it were osteitis fibrosa disseminata, it is very likely that there would be cysts in the hands as well, since the cysts tend to run up and down one limb.

I do not believe there is any question about the diagnosis. Probably, I am away out on a limb, but I should not consider any other diagnosis than Paget's disease. The x-ray film is absolutely characteristic. There is a sharp line of demarcation between the abnormal and the normal bone. The phosphatase level fits in very well. I do not know of any lesion other than Paget's disease that would give so much elevation in phosphatase for such a small lesion. I presume he had no bone lesions elsewhere.

DR. TRACY B. MALLORY: None were discovered.

DR. ALBRIGHT: The question comes up. Why did he have Paget's disease? Can Paget's disease develop in a fracture? I have never known of a case where this has been proved to occur. One often gets the history of fracture and, later on, full-blown Paget's disease in the same region, but in such cases x-ray films have never been available in my experience to show that Paget's disease was here at the time of the fracture.

I do not believe we have to consider sarcoma. We always worry about it when the fractures of Paget's disease begin to occur. I see no evidence of it here. Furthermore, the phosphatase should have been higher. However, let me take another look at these films with the sarcoma idea in mind. Where was the fracture?

DR. HOLMES: I cannot see it in these films, which I agree with Dr. Albright are characteristic of Paget's disease.

DR. ALBRIGHT: That is all I have to say and it is probably too much.

DR. MALLORY: Are there any other expressions of opinion?

DR. AUB: I think one has to consider the possibility of localized bone cyst, with change in shape because of the two previous fractures. Is that possible?

DR. ALBRIGHT: The phosphatase is too high.

DR. AUB: Yes, but if he had a fracture, it might go up.

DR. ALBRIGHT: It will take a good microscopic section to tell which it is anyhow.

DR. MALLORY: What would you say about bone cyst, Dr. Holmes?

DR. HOLMES: One might consider it in view of the history of multiple fractures. There are certain things here to make one think of it. The explanation of the peculiar deformity I should attribute to fracture; it is very characteristic of Paget's disease. If it is not that, I do not know what it is.

DR. ALBRIGHT: The first fracture came too late in life for one due to bone cyst, which usually fractures earlier.

DR. MALLORY: The great problem in these peculiar bone conditions is to establish a diagnosis by any means, and the question may well be raised whether the x-ray or histologic diagnosis is more reliable.

CLINICAL DIAGNOSIS

Bone cyst, with pathologic fracture.

DR. ALBRIGHT'S DIAGNOSIS

Paget's disease of bone.

ANATOMICAL DIAGNOSIS

Fibrocystic disease of bone.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was operated on by Dr. Henry C. Marble, who opened into what he believed to be a characteristic bone cyst. He curetted out a considerable amount of soft, gritty material. This was seen by several pathologists, one of whom said it was Paget's disease, but later retracted this diagnosis; one said it was fibrous dys-

plasia of bone; one could make nothing out of it but callus and repair. The cyst was packed with bone chips, and the patient made a fair recovery, went back to work and was quite well for a six-year interval. He then had another pathologic fracture and came in again. More x-ray films were taken on this entry, which Dr. Holmes will now show.

DR. HOLMES: They are poor films, and I cannot make much out of them. They are all taken through plaster and are overexposed.

DR. MALLORY: But there is no doubt about the fracture at that time.

DR. HOLMES: No; it is nice to have one thing about which we are certain.

DR. MALLORY: On the second occasion the bone was explored, and again, a cyst was reported by the surgeon. Once more the gritty material was curetted out, and again, the cavity was packed with bone chips. On this occasion Dr. Castleman considered very strongly the possibility of sarcoma. I disagreed, as did Dr. Granville A. Bennett and Dr. Henry L. Jaffe, to whom we sent the sections. Dr. Bennett having seen these sections and having reviewed the first ones is now convinced that the diagnosis of Paget's disease was erroneous. He is inclined to think that it is a fibrocystic process, whatever that may be. Dr. Jaffe thinks the most probable diagnosis is bone cyst. No one is willing to support Paget's disease.

DR. WILLIAM B. BREED: What do you think it is?

DR. MALLORY: I would like to make it fibrous dysplasia.

DR. ALBRIGHT: Paget's disease is both fibrous and dysplastic. I will grant you that.

DR. MALLORY: Would one in a case of Paget's disease find gross bone cysts filled with fluid? The description that the surgeon has given us is rather inadequate. I confess the fragments that we received following the curettage give little idea of the gross pathology. We have some good sections for histologic examination, however, and they do not look like Paget's disease.

DR. ALBRIGHT: An x-ray man calls any circumscribed bone lesion without calcium a cyst. Pathologists have to have fluid to call it a cyst, whereas a surgeon calls any fibrous tissue a cyst.

DR. MALLORY: Our sections showed mostly fibrous tissue and spicules of osteoid, with multiple very small cysts scattered through the tissue.

DR. ALBRIGHT: I should have to see it under the microscope. Have x-ray films of the bones of the forearm been repeated?

DR. MALLORY: No. The diagnosis I have to make is fibrocystic disease of bone. It certainly does not look like Paget's disease.

DR. HOLMES: If you look at the case from another angle, it is apparent that everyone disagreed except the radiologists and Dr. Albright. I obtained different opinions from several pathologists, so I think the diagnosis is Paget's disease. The majority rules!

DR. MALLORY: This is a very satisfactory result for the clinicians because we cannot prove we are wrong.

DR. ALBRIGHT: I should still like to see a section in the radius.

* * *

DR. ALBRIGHT (subsequent note): It has occurred to me that the biopsies were all taken from the site of the fractures. I think this explains the typical mosaic structure of Paget's disease, which was not found. The mosaic structure, of course, is one distinguishing feature between Paget's disease on the one hand, and osteitis fibrosa localis (bone cyst) and osteitis fibrosa disseminata on the other. I also looked up this patient and had serum phosphatase determined on November 1942, two months after the fracture. It was 1.5 Bodansky units per 100 cc. I therefore think must attribute the high phosphatase to the underlying Paget's disease and not to the fracture.

CASE 29032

PRESENTATION OF CASE

A sixty-year-old widowed telephone operator admitted to the hospital because of convulsions and loss of consciousness of two hours' duration.

The patient was in good health until two three weeks before entry, when she developed persistent, vague nausea and epigastric cramps. During this time she lost about 10 pounds in weight. Four hours before entry, when she was aroused from sleep to eat supper and go to her usual night work, she complained of numbness of hands. It was noted that her head was deviated to the right and that she seemed preoccupied. An hour later, she suddenly fell off her chair and had a generalized convulsion, lasting about seven minutes, in the course of which she lost consciousness, frothed at the mouth, bit her tongue and was incontinent. She remained unconscious and had two more convulsions, which were similar but first although more severe. A physician gave an injection of "morphine," pried a speculum from the patient's mouth and referred her to the hospital.

The family history was negative. The patient was previously healthy because of a heart murmur, which was frequently accepted. About a month before she was thought to have

She had had an uneventful menopause a year before entry.

In the two hours following admission the patient was unconscious. Her jaws remained firmly clenched on a mouth gag, and her head was turned toward the right. The extremities were motionless, except during two convulsions, the first left sided and the second generalized. There was incontinence of urine. In the next hour the patient recovered consciousness sufficiently to answer questions. During this time the left arm and leg were completely flaccid, with positive Hoffmann and Babinski reflexes. Tendon reflexes were exaggerated in the left leg. The neck was somewhat resistant to flexion. There was left-sided facial weakness of the central type. In the next half hour or hour the patient became mentally clear except for slight disorientation, and was able to converse freely. The signs of left facial paralysis disappeared, and the patient was able to move the left arm and leg. There was a suggestion of grasp reflex in the left hand, but other abnormal reflexes were no longer present. The fundi were negative, and the external ocular movements and papillary reactions normal. The tongue was bruised and lacerated, and could be protruded in the midline. The neck was no longer stiff. The lung fields were clear. The heart was enlarged slightly to the left. The heart sounds were of good quality, with a systolic murmur audible all over the precordium. A cardiac consultant made a diagnosis of moderate aortic regurgitation. The abdomen was obese, with no palpable masses. The pelvis was essentially normal.

The blood pressure was 170 systolic, 80 diastolic. The temperature was 100.5°F., the pulse 115, and the respirations 22.

Examination of the blood showed a red-cell count of 4,570,000, and a white-cell count of 11,900 with 92 per cent polymorphonuclears. The urine showed a +++ test for albumin. The blood Hinton reaction was negative. The nonprotein nitrogen was 26 mg. per 100 cc. An electrocardiogram showed unusually high P and T waves, but seemed within normal limits.

A lumbar puncture during the middle period of semiconsciousness gave clear colorless fluid under an initial pressure of 250 mm., with normal dynamics; it contained 237 red cells per cubic millimeter and gave a + test with ammonium sulfate. The total protein was 246 mg. per 100 cc.; the gold-sol curve was 5555555554. The spinal-fluid Wassermann reaction was unsatisfactory in one examination and anticomplementary in another.

A roentgenogram of the skull showed marked bilateral thickening of the inner table of the frontal bone. There were no other unusual areas of cal-

cification. The posterior clinoid processes were calcified. The sella was not enlarged.

There was evidence of a left homonymous hemianopsia on the morning after admission, but two days later the visual fields were normal. The patient remained slightly dazed. The temperature remained about 100°F. On the fifth hospital day the patient developed a stiff neck and had a series of convulsions that could not be controlled by luminal or rectal ether. After this, she passed into progressively deepening coma, and died on the eighth hospital day without regaining consciousness. There was terminal rise in temperature to 105°F.

DIFFERENTIAL DIAGNOSIS

DR. HENRY R. VIETS: The past history does not disclose any definite disease. The heart murmur that she had many years previously and that caused her to be turned down by a life-insurance company, although later accepted, can only be put down as a possible indication of valvular disease. The history of so-called "stomach ulcers" is even more vague. We have a note, moreover, that she was in good health a few weeks before the onset of her illness, and we know that she was working nights as a telephone operator even though her age was sixty. These facts would lead me to believe that she must have been in more than average health.

She developed persistent although vague nausea and epigastric cramps two or three weeks before the sudden onset of her epileptic attack. She had also lost 10 pounds in weight. These symptoms are not particularly suggestive of intracranial disease although they may denote some interference with the vagus nerves. Her weight is not given, but she is described as obese. This fact leads us to minimize the loss of 10 pounds. In a patient of slight weight, such a loss would be of much more importance.

We now come to the actual onset of a rather remarkable train of symptoms. The first symptom in the present illness was numbness of the hands. This was followed by some mental confusion or at least something that is described as a preoccupied condition with a deviation of the head to the right. The numbness of the hands is not particularly suggestive from the diagnostic point of view; the turning of the head to the right might indicate a spasm of the left sternomastoid muscle, and the preoccupation some vague mental state. After an hour she suddenly developed a generalized convulsion of severe degree, for it exhibited all the signs of marked epilepsy including loss of consciousness, frothing at the mouth, biting of the tongue and incontinence, as well as a sudden fall

off a chair. This was followed, moreover, within an hour or two by two more similar but even more severe convulsions, a condition of status epilepticus indicating a severe degree of cerebral dysfunction. Even after the patient entered the hospital she was unconscious and her masseter muscles were in spasm, with her head turned to the right. The convulsions continued, and then for the first time it is noted that one of them was on the left side of the body, thus corresponding with the turning of the head to the right, which was one of the earliest symptoms. Within an hour she recovered consciousness enough to answer questions. The whole episode of status epilepticus lasted six hours punctuated by various seizures. These left her with a left hemiplegia of the usual flaccid type, thus indicating the severity of the lesion, and with the ordinary positive Hoffmann and Babinski reflexes. For the first time it was noted that the neck was rather stiff, suggesting the presence of some foreign substance in the cerebrospinal fluid, probably hemorrhage.

Slowly the patient recovered consciousness and the paralysis disappeared, leaving her with a grasp reflex for a time, a common temporary residual of hemiplegia. The examination could then be made more in detail, and it was found that the pupils reacted normally and that there was no paralysis of the extraocular muscles or signs of choked discs. The neck, too, was no longer stiff; but we are not informed when this was discovered, and it is therefore difficult to say whether the absence of stiffness was subsequent to the lumbar puncture. We know that fluid was withdrawn at some time, but there again the timing is vague for it only states the "middle period of semiconsciousness." We presume this was on the evening of her illness, but the tap may have been performed later. The pressure was moderately increased, and there were over 200 red cells—whether they were crenated is not disclosed in the record. The total protein was ten times normal, and the gold-sol curve markedly affected. In spite of the fact that the fluid was colorless, there is every indication that considerable blood had appeared in the subarachnoid space some time prior to the puncture. It is important to know exactly when the puncture took place, for its timing is as valuable as the findings disclosed by examination of the sample. The Wassermann reactions were unsatisfactory, presumably because of the blood in the fluid. The other laboratory reports are not particularly helpful. A large amount of albumin in the urine is often found in cases of hemorrhage in the nervous system, particularly those of the subarachnoid variety. So far as I know this has not been explained. The low non-

protein nitrogen tends to rule out any chronic kidney condition. General examination showed moderate enlargement of the heart, with slight signs of aortic regurgitation. The electrocardiogram, too, was within normal limits, and I cannot see that the roentgenogram was helpful. The left homonymous hemianopsia is part of the left hemiplegia, only sensory rather than motor, and I presume that at the height of the left-sided motor paralysis there probably was a left hemianesthesia. This would be impossible to test for in her condition of semicoma.

The patient did fairly well in the hospital for three or four days, although always somewhat mentally confused. The signs of hemiplegia and hemianopsia disappeared. On the fifth day she again developed a stiff neck, indicating a fresh outpouring of blood into the subarachnoid space. This was followed by another series of convulsions. Subsequently coma developed, and the patient died on the eighth hospital day without regaining consciousness. There was a terminal rise of temperature.

The sudden onset of severe epilepsy leading to cerebral attacks can only indicate a severe intracranial lesion. We have evidence, on account of the left hemiplegia, that at least the major portion of the lesion was on the right side of the brain. This was confirmed, moreover, by the later discovery of homonymous hemianopsia. Sudden epilepsy is most likely due to cerebral thrombosis, although it may be the result of cerebral hemorrhage, particularly if the hemorrhage is cortical or meningeal. The slow onset of this patient's condition in which she had symptoms at least an hour before the generalized convulsion, is strongly suggestive of thrombosis rather than of hemorrhage. Although theoretically we assume that thrombosis is more likely than hemorrhage, we have the definite fact that there was blood in the spinal fluid. The bleeding, moreover, was sufficient to cause some stiffness of the neck even on entry to the hospital. Subsequently the spinal fluid was indicative of a condition in which blood must have been present in large amounts at one time. This is the only way one can account for the increase in total protein to nearly ten times normal and the marked change in the gold-sol reaction. Although the red-cell count was only 237 at the time the tap was made, one has every justification in assuming that many more cells were in the fluid at some previous time, perhaps sufficient to make the fluid red in color. That the initial lesion was hemorrhagic in nature and subsequently bled again is indicated by the finding of stiffness of the neck and convulsions on the fifth hospital day. We thus may assume, I think, that a hemorrhagic lesion of some

sort was sufficient to cause the symptoms. Was this hemorrhage primarily in the subarachnoid space or within the cerebrum itself?

The transient nature of the hemiplegia and the homonymous hemianopsia suggest that whatever lesion in the right side of the brain caused these two findings, was far from permanent. This is, therefore, not suggestive of a thrombosis or of an intracerebral hemorrhage. A surface hemorrhage, however, would give such findings, for the pressure might rapidly be adjusted. Such a hemorrhage, moreover, would account for the cortical irritation giving rise to the status epilepticus. Although a thrombosis in general gives rise to epilepsy more frequent than does hemorrhage, that comparison is usually made with intracapsular hemorrhage and not with meningeal hemorrhage, which is in evidence here.

Embolism seems even more unlikely. In the first place, the history of heart disease is vague and even the examination disclosed only a moderate lesion that was not suggestive of activity. To be sure an aortic valvular lesion may lie dormant and subsequently a portion may come away and act as an embolus. This would not in all likelihood account for the hemorrhage into the subarachnoid space, and most cardiac emboli that enter the brain do so on the left side and give rise to right hemiplegia with its accompanying aphasia. Embolic lesions, moreover, are likely to be more fixed and not so transient in nature. I therefore believe that, although we may find evidence of cardiac disease, such as an aortic lesion, it is not likely that this lesion was the cause of death, even in a secondary manner through cerebral embolism.

Finally, we have to consider the likelihood of an aneurysm as the etiology of the subarachnoid hemorrhage. The onset of the illness is not quite so prompt as we find in most cases of bleeding aneurysm. We have, however, plenty of evidence that aneurysms may leak slowly and sometimes give symptoms for two or three weeks in advance of their rupture, such as might well have occurred in this case. The bleeding at the time of rupture may be sufficient to give a generalized convulsion. Apparently more blood appeared on the right side than on the left, and therefore the generalized convulsions were mixed with left-sided attacks. This condition quieted down; but after five days it was resumed in the hospital, and in three days death ensued. There is no indication where such an aneurysm arose. We must think of the usual position of these lesions in the circle of Willis, but in this case there is nothing to give us a lead concerning what part of the circle was affected.

We might be dealing, of course, with bleeding from some lesion other than aneurysm. Occasional-

ly we find symptomless gliomas that disclose themselves by bleeding. That is a possibility but a rare one. There are also vascular tumors such as hemangiomas, long quiescent, that suddenly announce themselves by bleeding into the subarachnoid space or into the brain. These lesions are rare, and although they are possibilities, in this case I do not believe we can make either diagnosis.

The diagnosis, therefore, is cerebral hemorrhage, possibly subarachnoid in type, more on the right side than the left. Aneurysm of a cerebral vessel is a strong possibility, with location not disclosed.

DR. EARLE M. CHAPMAN: Did you say that embolism in heart disease was statistically commoner on the left side of the brain than on the right?

DR. VIETS: Yes; I think that is right.

DR. JOST MICHELSEN: Do you think the combination of aortic regurgitation, the high protein in the cerebrospinal fluid and the gold-sol curve suggests a syphilitic lesion?

DR. VIETS: A gold-sol curve with so many S's in it always indicates that there has been blood in the spinal fluid. That is the only thing I know of that can give a gold-sol curve like this one. The high protein also means that there must have been some blood in the fluid. Whether that came from a vascular lesion other than aneurysm or hemangioma, I do not see how we can tell. There is no history up to the present illness that indicates that the patient had a hemangioma. She had no cerebral symptoms.

DR. MICHELSEN: If hemorrhage accounted for the high protein, would they not have seen a discoloration of the spinal fluid?

DR. VIETS: That is why I was interested in when the cerebral spinal fluid was examined.

DR. CHARLES S. KUBIK: It was done on the day after the patient was admitted.

DR. VIETS: That seems almost too soon for color to appear in the spinal fluid. A little yellow tinge I am quite sure is missed very frequently. If it is bright red anyone sees it.

DR. G. COLKET CANER: The facts that she lost 10 pounds in weight and had nausea and epigastric cramps, then woke up complaining of numbness of both hands give a vague impression of multiple lesions. Those things, together with the fact that she had a little blood and a high protein in her spinal fluid, indicating previous hemorrhage, make one think of the possibility of metastatic disease. There is not much evidence of it here, but there is a slight indication of multiple lesions.

DR. KUBIK: When I saw the patient I was impressed by the stiff neck and the red cells in the spinal fluid, thought of subarachnoid hemorrhage, wondered about the possibility of aneurysm but

ended up by saying that nothing I could think of fitted the picture very well. The important thing, it seemed to me, was to control the seizures, using ether anesthesia if necessary. Status epilepticus, regardless of the underlying condition, is likely to result in death, apparently from pulmonary congestion and edema. The ether should be given by inhalation.

Dr. Paul D. White saw the patient, and said:

A moderate amount of aortic regurgitation, dating back evidently fifteen years and therefore doubtless rheumatic in origin, is the only clear-cut finding on physical examination. This lesion is a good background for subacute bacterial endocarditis, of which, however, there is as yet no other evidence.

Red cells in the spinal fluid are often observed with cerebral complications of subacute bacterial endocarditis.

In view of what was found on post-mortem examination I am surprised that there were no white cells in the spinal fluid. I think that there must have been white cells.

Dr. VIETS: Of course that would change the picture a good deal.

CLINICAL DIAGNOSES

Cerebral hemorrhage.

Aortic regurgitation.

Bronchopneumonia.

DR. VIETS'S DIAGNOSIS

Cerebral hemorrhage, possibly subarachnoid
(? aneurysm of cerebral vessel).

ANATOMICAL DIAGNOSES

Neurosyphilis, meningovascular.

Syphilitic aortitis, with aneurysm.

Cardiac hypertrophy.

Pulmonary edema and congestion, slight.

Frontal hyperostosis.

Fibroid tumors of uterus.

PATHOLOGICAL DISCUSSION

Dr. TRACY B. MALLORY: Will you tell us about the cerebral findings at autopsy, Dr. Kubik?

Dr. KUBIK: There was no hemorrhage, no evidence of bleeding anywhere, either on the surface or within the substance of the brain, and no arterial occlusion or softening. There was one clue—a roughening of the ependyma of the floor of the fourth ventricle that was a little different from the usual so-called "granular ependymitis." This suggested neurosyphilis as a likely possibility, and the diagnosis was confirmed by microscopic sections.

There was an exudate of lymphocytes and plasma cells in the subarachnoid space over the brain stem and cerebral hemispheres. In the cerebral cortex and also in the cerebellum there

were scattered areas in which there was extensive perivascular infiltration with lymphocytes and plasma cells, nerve-cell degeneration and gliosis. No doubt there were many other areas like that. Some of these vessels were occluded. In other parts the cortex did not look very abnormal. There was an endarteritis of the medium-sized arteries in the subarachnoid space of the brain stem. I am not sure whether the diagnosis is general paresis or meningovascular syphilis but favor the former for the cortical pathology.

Dr. MALLORY: On examination of the cardiovascular system we found confirmatory evidence for the diagnosis of syphilis. The aortic valve showed a distinct separation of the cusps at the commissures, and the coronary arteries appeared to take their origin 2 or 3 mm. above the upper margin of the aortic cusps, thereby indicating that attachment of the cusp had gradually been lowered, as it so characteristically is in syphilitic involvement of the aortic valve. The ascending aorta was moderately dilated and showed a great deal of wrinkling. On microscopic examination there were focal destruction of the media and perivascular infiltration of lymphocytes in the adventitia and also in the vascularized media. I think that both the cerebral and vascular findings are characteristic enough to permit us to make a positive diagnosis even without serologic support. There was a slight pulmonary congestion and edema, secondary, I believe, to the status epilepticus. A coincidental lesion was hyperostosis of the frontal bones; I do not believe it played any part in the symptomatology.

Dr. CHAPMAN: Did you do a Hinton test on the blood obtained at autopsy?

Dr. MALLORY: No; such tests are usually not very satisfactory, since they are likely to give anti-complementary reactions.

Dr. VIETS: Do you want to comment on status epilepticus as the terminal event in a general paretic?

Dr. KUBIK: I think that a patient may die of status epilepticus quite apart from the underlying disease, which may be neurosyphilis, brain tumor or something else. Every effort should be made to stop the convulsive seizures and to do so as quickly as possible. The usual anticonvulsive drugs often have little or no effect on the convulsions, and when given in large doses, may do considerable harm. Ether anesthesia, in my experience, has been very effective, and I believe that it is also less harmful. It acts quickly and surely and is rapidly eliminated.

I should suppose that in the present case the patient died as a result of status epilepticus, with pulmonary congestion and edema as the chief cause of death.

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PRESIDENT-EMERITUS LOWELL AND MEDICAL EDUCATION

THE late A. Lawrence Lowell, president-emeritus of Harvard University, always took a great interest in the Harvard Medical School. In June, 1939, he made some informal remarks on medical education to the Class of 1914 on its twenty-fifth anniversary. These remarks were subsequently published in the March 21, 1940, issue of the *Journal* and were commented on editorially in the same issue. This article reflects his considered opinion regarding the education of physicians.

Mr. Lowell always maintained that it was unwise to argue with an expert on the expert's own ground. Consequently, his contributions on medical education were by way of suggestions rather

than by declared policies. Mr. Eliot used the phrase, "prodigious advances in medical science," whereas Mr. Lowell referred to the "vast improvement in medical education." Perhaps Mr. Lowell's most concrete suggestion was the introduction of general examinations at the Harvard Medical School in 1914. These were largely based on the type of examination then employed at Harvard College.

Mr. Lowell was always distressed by the length of medical education. He once referred whimsically to the possibility that a man would be forced to retire on account of age just before he completed his training. He had the feeling that there were needless attempts to cover too much ground and that, of necessity, much of the material was forgotten by the student before he had any opportunity to put it to use. He claimed that there was a tendency to add the new to the old without sufficient effort to eliminate some things no longer needed, and believed that it should be possible to solidify and simplify the curriculum, in which he included the time spent in hospitals.

He was always very fond of the following anecdote. His brother once complained bitterly to his father, "Doctors really know very little." His father replied, "Yes, that is true, but the doctors know a little more than we do and so we find them valuable." Mr. Lowell would then go on to say that he had seen the situation entirely changed and that such a remark would not be appropriate today. He added, however, that the change, unfortunately, seemed to have been made at the cost of the withdrawal, as compared with former times, of the medical profession from civic affairs, to which they could contribute so much.

THE PERIOD OF RESISTANCE

MANY children—indeed it would be safe to say nearly all children—some time in their early, preschool years of life, enter a period of stubbornness, contrariness and spitefulness that, if improperly handled, may miscolor the rest of the stages of their lives and set a pattern for their maturer

years. By no means all children constitute serious problems at this period, but it is fair to say that any child worth the raising constitutes somewhat of a problem.

This period has for years been called the "neglected age" of childhood, the cause of the neglect lying quite reasonably in the attitude of the child toward interference with his independent desires; Benjamin,^{*} whose studies at Johns Hopkins University represent the most recent contribution to the problem, calls it the "period of resistance."

Underlying the spite and negativism that make up the chief characteristics of this period, with their varying expressions of misbehavior from thumb-sucking to bed-wetting, from temper tantrums to encopresis and head-rocking, is always a basis of anxiety or inner insecurity—the result of an unsuccessful transition from infancy to early childhood. All human personality difficulties stem from a combination of hereditary and environmental factors, as the architecture of any building must be determined by the type of building materials available, as well as the skill of the architect. With due allowance for the material utilized, these poor results are obtained from a training that does not give enough independence, or destroys self-confidence by punishment and frustration.

Benjamin's plea is for a family structure that recognizes the rights of all its members from the beginning. He writes:

Real democracy begins at the beginning, when neither parental nor infantile despotism should be allowed to govern the social unit which is the home. Disturbing rebellion, which is still so frequent in children . . . has no opportunity to flourish in an atmosphere of good sportsmanship, reasonable compromise, reciprocity and mutuality.

Unwholesome remonstrance can be prevented. Such an attitude is over and above the safest guarantee for the rearing of self-dependent, conforming, considerate, truly free and democratic Americans.

Undoubtedly, a fuller appreciation of this precarious period in early childhood by both physicians and parents will do much to prevent many of the difficulties that arise in later life.

^{*}Benjamin E. The period of resistance in early childhood *Am. J. Dis. Child.* 63:1019-1077, 1942

MEDICAL EPONYM

SPRENGEL'S DEFORMITY

Otto Sprengel (1852-1915), chief surgeon at the Children's Hospital of Dresden, described "Die angeborene Verschiebung des Schulterblattes nach oben [Congenital Upward Displacement of the Shoulder Blade]" in the *Archiv für klinische Chirurgie* (42:545-549, 1891). A portion of the translation follows:

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R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

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MICHAEL A. TIGHE, *Secretary*

* * *

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The Office of the Surgeon General has informed me that the United States Public Health Service is in need of an average of twenty-five physicians per month for Coast Guard and War Shipping Administration work, and others for the States Relations Division and miscellaneous assignments.

These physicians will be commissioned in the United States Public Health Service Reserve in the grade of assistant surgeon, or passed assistant surgeon if over thirty-

three years of age Application forms will be available at this office

It will be appreciated if you will bring this matter to the attention of your members or affiliates and urge any who are interested to communicate with me

Sincerely yours,

R P SANDIDGE, *Senior Surgeon*
Medical Officer in Charge

United States Marine Hospital
Boston

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

MISCELLANEOUS

Of the 5 cases of ruptured uterus that occurred during 1941, the first was that of a thirty four year-old woman who had had no prenatal care during this pregnancy and whose history does not relate whether there had been any previous pregnancies. She was first seen at home as an emergency because of profuse vaginal hemorrhage when about five months pregnant and immediately taken to the hospital by ambulance. Bleeding did not recur. X-ray films taken four days after admission revealed no evidence of fetal bones. Three days later a curettage was performed, the pathological diagnosis of which was "degenerative decidua tissue and hyperplastic endometrium". The patient's temperature rose immediately after the curettage; two days later the abdomen became distended, and death occurred the following day. Autopsy showed peritonitis, with rupture of the uterus on the right, the opening being just large enough to admit the passage of a No 3 dilator. A macerated fetus of five months, with the placenta, was found in the right lower quadrant. The rupture of the uterus was probably traumatic. It is very likely that the pregnancy was abdominal, since it is inconceivable that the fetus and the placenta could have passed into the abdominal cavity through so small a rupture in the uterus. The diagnosis was undoubtedly missed; if the proper diagnosis had been made when the patient was first seen, and a laparotomy performed, this catastrophe could probably have been prevented.

The second patient, a thirty one year old woman who had had one previous miscarriage, first consulted her physician when about four months pregnant; she complained of pain in the shoulder, and several hours later went into profound shock. The diagnosis of ruptured ectopic pregnancy was made, and the patient was sent to the hospital, arriving pulseless and without a demonstrable blood pressure, death occurred very shortly thereafter. Autopsy showed rupture of the uterus, with a four month old fetus still in the sac and a

placenta accreta. The patient's past history was negative, except for the previous miscarriage when three months pregnant. Spontaneous rupture during the fourth month of pregnancy is a most unusual occurrence. It is possible that if the proper diagnosis had been made when the patient was first seen, before she went into shock, abdominal operation would have been successful.

The third patient, a forty-year-old para II who had had excellent prenatal care, went into labor at term. She had very severe pain during labor and was delivered normally ten minutes after admission to the hospital. The baby was dead, and an excessive hemorrhage followed delivery. The patient became pulseless and went into shock, and died ten minutes after delivery of the placenta. Autopsy proved the cervix to be torn deep into one vault, the tear extending into the uterus and broad ligament; the uterine artery on the right was severed. There is no note that pituitrin had been used, and it is possible that the cervix was so filled with scar tissue from the previous delivery that the tear into the broad ligament resulted from the rupture of undilatable scar tissue. This was an unfortunate case but one in which in all honesty the blame cannot be laid to inadequate or overzealous obstetrics.

The fourth case occurred in a thirty six-year-old patient who had had a previous cesarean section for placenta previa. When about thirty six weeks pregnant she complained of severe abdominal pain and was immediately sent to the hospital. A general surgeon was called as consultant, and $\frac{1}{4}$ gr of morphine was ordered. The patient died undelivered two hours later, autopsy showing that the uterus had ruptured along the scar of the previous section. The baby was lying in the abdominal cavity. There was no excuse whatever for this fatality. One quarter of a grain of morphine has never saved the life of a patient with a ruptured uterus.

The fifth patient, a thirty eight-year old primipara who was delivered at term by low forceps, had a severe post partum hemorrhage, examination revealed an incomplete rupture of the uterus. Supravaginal hysterectomy was performed, and the patient was transfused four times. The signs and symptoms of peritonitis developed thirty-six hours post partum, and the patient died of peritonitis on the fourth day. Rarely, the cervix does rupture in a normal delivery and does cause profuse post-partum hemorrhage. From the record one would infer that the operation was not difficult, and hence not the cause of the rupture. Everything possible in the way of treatment was done for this patient. A specific diagnosis was made, the patient was

years. By no means all children constitute serious problems at this period, but it is fair to say that any child worth the raising constitutes somewhat of a problem.

This period has for years been called the "neglected age" of childhood, the cause of the neglect lying quite reasonably in the attitude of the child toward interference with his independent desires; Benjamin,* whose studies at Johns Hopkins University represent the most recent contribution to the problem, calls it the "period of resistance."

Underlying the spite and negativism that make up the chief characteristics of this period, with their varying expressions of misbehavior from thumb-sucking to bed-wetting, from temper tantrums to encopresis and head-rocking, is always a basis of anxiety or inner insecurity—the result of an unsuccessful transition from infancy to early childhood. All human personality difficulties stem from a combination of hereditary and environmental factors, as the architecture of any building must be determined by the type of building materials available, as well as the skill of the architect. With due allowance for the material utilized, these poor results are obtained from a training that does not give enough independence, or destroys self-confidence by punishment and frustration.

Benjamin's plea is for a family structure that recognizes the rights of all its members from the beginning. He writes:

Real democracy begins at the beginning, when neither parental nor infantile despotism should be allowed to govern the social unit which is the home. Disturbing rebellion, which is still so frequent in children . . . has no opportunity to flourish in an atmosphere of good sportsmanship, reasonable compromise, reciprocity and mutuality.

Unwholesome remonstrance can be prevented. Such an attitude is over and above the safest guarantee for the rearing of self-dependent, conforming, considerate, truly free and democratic Americans.

Undoubtedly, a fuller appreciation of this precarious period in early childhood by both physicians and parents will do much to prevent many of the difficulties that arise in later life.

*Benjamin, E. The period of resistance in early childhood. *Am. J. Dis. Child.* 63:1019-1077, 1942.

MEDICAL EPONYM

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were discrete nodules or groups of interstitial cells locally replacing or displacing the seminiferous tubules. Of these there were 13 cases. There were only 3 cases of malignant tumor, which is regarded as an increase of interstitial cells with anaplasia, destruction of tubules and metaplasia. The main features distinguishing these groups are the number and pattern of distribution of the cells. The histologic characteristics, except in the case of malignant tumors with metastases, do not offer enough variation to distinguish between the various types of growth in the presence of the meager clinical data available. Furthermore, there is no satisfactory method of determining the number of interstitial cells in the normal person, because of the variability in the number, size and distribution of the seminiferous tubules, blood vessels, nerves and connective-tissue cells. The "normal number" of interstitial cells is only a visual impression gained by microscopically comparing sections from a series of three hundred and seventy testicles obtained at autopsy and from surgical material. Hormonal changes were relatively few except in children in whom there was precocious puberty with gynecomastia. For the most part ketosteroid determinations were not done. However, in one case report by Mason, the Aschheim-Zondek test was positive in a 1:50 dilution.

The last paper was given by Dr. Shields Warren and was entitled "Bone-Marrow Changes following the Administration of Radioactive Phosphorus." The report was based on 8 patients who had come to autopsy a varying length of time following the administration of radioactive phosphorus, either orally or intravenously, as disodium phosphate. The changes induced in the bone marrow do not differ significantly from those seen in other types of radiation, such as deep x-ray therapy. The changes ranged from very marked depletion of the marrow with almost no abnormal cells and few normal cells to practically no changes, except for minor evidence of damage to cells of the granulocytic series and to some of the megakaryocytes. In most cases there was radiation effect in all marrow elements. As evidenced by examination of the peripheral blood and bone marrow, the general effect of radioactive phosphorus seems to be injury to all marrow elements, with particular effect on the more rapidly proliferating cells. These cases received small doses of low intensity, having been given 2 millicuries at ten day intervals with the dose gradually spreading to once every three to six months. The phosphorus is taken up by the rapidly growing cells, and is accompanied by a drop of the total white-cell count, with a greater percentage of mature cells in the peripheral blood, and a decrease in the number of erythrocytes and platelets. If the dosage is sufficiently small, the effect may be selective on the leukemic cells. In summary, Dr. Warren said that the number of cases is not sufficient for clinical evaluation and that the advantages to date are of minor importance. The latter are as follows: there is no radiation sickness; it is easy to maintain the proper level by either oral or intravenous administration; and treatment can be carried out without bringing the patient to the hospital. It is also quite probable that the dose is concentrated at the point of disease. In the discussion it was brought out that in patients given large doses the effect on the marrow approaches that seen in aplastic anemia and that damaged cells, at least those showing evidence of vacuolization, are found in the circulating blood. Hemosiderin was found in rather abundant amounts, but the amount was not thought to have any clinical significance.

BOOK REVIEWS

Four Treatises of Theophrastus von Hohenheim, Called "Paracelsus." Translated from the original German, with introductory essays. By C. Lillian Temkin, George Rosen, Gregory Zilboorg, M.D. and Henry E. Sigerist, M.D. Edited, with a preface, by Henry E. Sigerist, M.D. 8°, cloth, 256 pp., with 1 portrait. Baltimore: The Johns Hopkins Press, 1941. \$3.00.

The character of Paracelsus was full of contradictions, — violent ones, — which explains why to some he has seemed no better than a besotted charlatan and to others little short of a sainted mystic. The truth — as it so often does — lies in the middle ground. The force of his personality and the originality of his mind cannot be denied. He quarreled so violently and persistently with his professional colleagues that he became an habitual outcast, and many of his writings were denied publication during his lifetime. Yet, he was the founder of chemical therapeutics; he wrote the first treatise on industrial medicine, which discussed miners and their ailments; and he attempted something in the direction of psychiatry and psychology. For the whole list of his contributions, one should consult a book on medical history. All in all his was a great part, and worthy of recollection.

He died four centuries ago, and this book is essentially a memorial volume. The four treatises, each translated by a different hand, are as follows: *Seven Defenseones*, an attempt to justify his views of medicine in opposition to those then prevailing; *On the Miners' Sickness and Other Miners' Diseases; Diseases That Deprive Man of His Reason*; and *A Book on Nymphs, Sylphs, Pygmies, Salamanders*, and so forth, which according to Professor Sigerist affords a good example of Paracelsus's philosophy and theology.

It is pleasant to have something besides hearsay about so important a man. But these treatises are not easy reading. There is much in them that seems obscure, but, as Professor Sigerist remarks in his preface, to translate Paracelsus into modern English would lose much of the original meaning. With all the difficulty, one can discern in the man a trait of shrewd medical observation and a pervading spirit of honesty of mind. And those facts alone are worth the learning.

Food and Beverage Analyses. By Milton A. Bridges, M.D., and Marjorie R. Mattice, M.S. Second edition, thoroughly revised. 8°, cloth, 344 pp., with 40 tables. Philadelphia: Lea & Febiger, 1942. \$4.00.

This second edition, revised and amplified by Professor Mattice after the death of Dr. Bridges, is intended as a reference book for clinicians, students, dietitians, nurses and those concerned with applied nutrition and dietetics. It aims "to provide analytical data on the largest possible number of food factors . . . presented in a readily understandable fashion." The bulk of the material consists of tables of the composition of foods and beverages; but there are also brief general discussions, including chapters on carbohydrates, proteins, fats, water, vitamins, acidity of foods, inorganic salts and alcoholic beverages. There is a glossary of vitamin terms, including the structural formulas of some of the more important vitamins. An extensive bibliography is appended. The figures for food analyses are partly collected from reports in the literature and partly from the authors' own work. They are undoubtedly reliable and as free from error as is humanly possible.

There is great call for such a collection of readily available food and beverage data, attested to by the haziness in the minds of many clinicians concerning food values, and the general tendency to pass all diet-making along to the dietitian. There is also a need for periodic additions to the available data, to include foods and products that are constantly being introduced. Only a few recent single publications meet these needs, notably Chatfield and Adams's *Proximate Composition of American Food Materials* (United States Department of Agriculture Circular No. 549—June, 1940) and the present volume, which is the more extensive.

Although knowledge of the exact composition of foods is most desirable, Bridges and Mattice are quick to point out that many, if not most, of the present analytical data are of necessity anything but exact. Naturally occurring foods vary widely in composition, and such factors as freshness, variable water content, differences in soils, processing and cooking make anything but average values impossible. Furthermore, there are varying factors in the absorption and utilization of some constituents. For example, if one eats spinach, which has a considerable calcium content but is also rich in oxalates, it not only supplies no available calcium but also makes unavailable much of the calcium in other foods ingested at the same time. Finally, there are technical difficulties in chemical analysis, and different workers report widely divergent figures for the same food factors. For example, the English workers, McCance, Widdowson and Shackleton, give figures for the crude-fiber content of foods that are consistently two to eight times higher than those of other workers.

Some data in these tables, although as accurate as possible, are of dubious applicability in dietetics. The acidity of foods as eaten, for example, has no relation to their final effect in body metabolism, as the authors note. Such tables could well be omitted.

If due account is taken of all these pitfalls in the figures, this volume will be of great value to everyone in the field of practical dietetics.

Clinical Hematology. By Maxwell M. Wintrobe, M.D., Ph.D. 8°, cloth, 792 pp., with 167 engravings and 7 colored plates. Philadelphia: Lea and Febiger, 1942. \$10.00.

This book is by far the best English text on the subject of clinical hematology. Crowded into its pages is a wealth of material, all carefully annotated and documented, and replete with references. The completeness of these references—author, title, volume and page—is an indication of the care with which the entire book has been written, from introduction to index, and is confirmatory of the author's reputation as a careful investigator of hematologic and nutritional problems.

In the last few years a wealth of new hematologic texts in English has appeared to fill the large gap formerly present in this field. Some, like that of Kracke, have had excellent illustrations with a rather indifferent text; others, like that of Haden, have quite frankly been written for the general practitioner and as such have been rather elementary in their scope. The monumental four-volume "handbook," edited by Downey, is somewhat unbalanced by its editor's histologic bias, with the result that the clinical articles are often subordinated and given but scant attention. Wintrobe, being primarily a clinician with both physiologic and histologic training, has been able to keep the proper balance between these fields and

has thus produced a first-rate work, which is difficult to criticize.

Descriptions of the blood-forming organs and of the blood cells are complete and free both from the unnecessary polemics regarding derivation of cells and the unique nomenclatures affected by both Osgood and Kracke. The chapter on macroscopic examination of the blood, including the various indices, is new for hematologic texts and reflects Wintrobe's pioneering efforts in this field. Anemia is first considered as a general physiologic problem, the matter of therapy receiving a 50-page section. In the chapters on the various specific diseases, two things stand out: the large number of references,—commonly seen only in monographic articles,—and the consideration of pathology and pathogenesis at the end of each chapter. Ordinarily, one would expect to find possible pathogenetic mechanisms first, pathology second, clinical features third, and treatment last. It must be conceded, however, that Wintrobe's arrangement detracts but little from the value of the book. The chapters on hemolytic anemia, sickle-cell anemia and Mediterranean anemia are excellent, far outranking similar chapters in other texts. Except for hypoprothrombinemia, the hemorrhagic diseases are well covered, as are the leukemias and leukocytic neoplasms. There is a brief but comprehensive chapter on the spleen.

In short, the reviewer has nothing but fulsome praise for Wintrobe's book. One might like a little less didacticism and a little more physiology here and there—but this is captious criticism.

Architectural Principles in Arthrodesis. By H. A. Britain, M.A., M.Ch. With a foreword by Harry Platt, M.D., M.S., F.R.C.S., F.A.C.S. (hon.). 8°, cloth, 132 pp., with 144 illustrations. Baltimore: The Williams and Wilkins Company, 1942. \$6.00.

In this small, superbly illustrated volume, an attempt is made to apply certain principles of architecture to the operation of arthrodesis. It is shown in drawings and photographs that stresses which may lead to failure in an attempted fusion of a joint can be combated by struts made from tibial grafts. The technic of applying such grafts to each joint during the operation of arthrodesis is described. The broad indications for arthrodesis that the author advocates, however, are not accepted in the United States. Here, arthrodesis, except in the case of tuberculosis, is used only as a last resort, but in the author's practice it is the primary operation in many disabilities. The majority of procedures appear to be sound, but the operations that the author performs for arthrodesis of the hip and the ankle seem to make the procedures unnecessarily long and difficult.

Hippocratic Medicine: Its spirit and method. By William A. Heidel. 8°, cloth, 149 pp. New York: Columbia University Press, 1941. \$2.00.

In the days of Hippocrates, Greek medicine, as well as Greek science, was intimately tied in with philosophy. The most significant Hippocratic contribution was, in the last analysis, a point of view—but one so valid that, in essence, it still holds after two and a half millenniums. In this pleasant little book, Professor Heidel discusses the methods, the manners and the posture of medicine in the fifth century B.C. It is not a "must" book, of course, but to read it will be a pleasure and a profit to any physician with a feeling for history and a reverence for the ideals of his profession.

(Notices on page x)

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THE OCCURRENCE OF COR PULMONALE IN CASES OF BRONCHIAL ASTHMA*

IRVING W. SCHILLER, M.D.,† ABRAHAM COLMES, M.D.,‡ AND DAVID DAVIS, M.D.§

BOSTON

THERE is no uniformity of opinion regarding the role of bronchial asthma in the causation of heart disease. Most authors hold that cardiac complications of this origin are uncommon.¹⁻³ On the other hand, it has been pointed out that bronchial asthma and its sequelae, pulmonary emphysema, often lead to right-ventricular hypertrophy and finally heart failure.⁴⁻⁶ The number of autopsied cases with bronchial asthma reported in the literature, however, is not large, and not all writers have recorded full data on the heart. For this reason, it is of interest to report the cardiac findings in 15 cases of bronchial asthma that came to autopsy. In addition, 54 patients were studied clinically to determine the incidence of cardiac abnormalities of this origin.

ANALYSIS OF DATA

Forty-six of these 69 ambulatory and autopsied patients were men; 23 were women. Fifty-nine (85 per cent) were past forty years of age. Forty-two (61 per cent) had had asthma for ten years or longer. The average duration of the disease was thirteen years. The cases were selected on the basis of the history, physical examination, blood studies and skin tests. A family history of allergy was present in 26 cases (38 per cent). Skin tests were positive in 46 cases (67 per cent), and an eosinophilia of 5 per cent or more was found in 22 cases (32 per cent).

Clinical Data

The histories and physical examinations of the 54 nonautopsied patients were studied to determine the presence or absence of congestive failure. Although in most patients dyspnea was an outstanding symptom, it could not be established that cardiac weakness was a factor except in 1 patient, who

later gave evidence of a cor pulmonale. Likewise, physical examination revealed no evidence of heart failure.

Teleroentgenograms were made in 46 cases. In 34 (74 per cent) the heart shadow appeared normal, in 7 (15 per cent) it was enlarged, and in 5 (11 per cent) the left ventricle was blunted and prominent. Six of the 12 patients with some cardiac enlargement had hypertension; an obvious cause for the enlargement was not found in the remaining 6.

The velocity of blood flow was determined by the Decholin method⁷ in 40 cases.⁷ The average normal circulation time with this method is 15 seconds. The readings in 37 cases (92 per cent) were within normal limits (average 12.8 seconds); in only 3 cases was the circulation time prolonged (22.0, 22.2 and 26.0 seconds, respectively). These 3 patients showed no clinical evidence of congestive failure. The electrocardiograms in 1, however, showed abnormally inverted T waves, and in another there was prolongation of the QRS interval. It has been shown that there is a tendency for the velocity of blood flow to be slightly increased in emphysema,⁸ and this was true in the vast majority of our cases. The occurrence of a prolonged circulation time in these cases, in the absence of any other cause, was considered suggestive evidence of beginning circulatory failure.

Electrocardiograms were available in 46 cases. Fifteen (33 per cent) of these were within normal limits. Thirty-one patients (67 per cent) showed the following abnormalities: prolongation of the QRS interval, 3 cases; inverted T waves in Leads 1 and 2, 7 cases; abnormalities in Lead 4, 3 cases; an abnormally deep Q wave in Lead 3, 2 cases; a deep S wave in Lead 2, 7 cases⁹; and auricular fibrillation, 1 case. Thirteen patients (28 per cent) showed left-axis and 6 (13 per cent) right-axis deviation. A tendency to right-axis deviation was

⁷Decholin Sodium was kindly supplied by Riedel-de Haen, Incorporated, New York City.

*From the Allergy Clinic of the Beth Israel Hospital.

†Instructor in medicine, Tufts College Medical School.

‡Chief of Allergy Clinic, Beth Israel Hospital.

§Instructor in medicine, Harvard Medical School, junior visiting physician and associate in research, Beth Israel Hospital

further noted in 4 other patients (9 per cent). The only abnormal finding in the electrocardiogram in 6 cases was left-axis deviation, and in 2 cases right-axis deviation.*

Autopsy Data

Autopsy data were available in 15 patients who died during the course of this study. A summary of the clinical and postmortem findings in these

years previously he began to have asthmatic attacks, which were more marked in warm and damp weather. These became progressively more frequent and severe. Two years before admission he began to complain of dyspnea on exertion and attacks awakening him at night. Ten months before admission he began to have swelling of the lower extremities and palpitation on slight exertion. All the symptoms became progressively more marked.

Physical examination on admission showed cyanosis of the lips and cheeks and a uniformly enlarged thyroid

TABLE 1. *Clinical and Autopsy Findings in 15 Cases of Bronchial Asthma.*

Case No.	Age	Sex	Duration of Disease, Yrs.	Duration of Cardiac Symptoms	Duration of Edema	Heart Weight, gm.	Heart Findings			Infarcts	Lung Findings				Cause of Death
							Ventricular Thickness		Coronary Arterio-sclerosis*		Chronic Bronchitis	Diffuse Fibrosis	Atherosclerosis	Microscopical Emphysema	
							Right	Left							
			Yr.	Yr.	mo.	gm.	mm.	mm.							
1	53	M	12	1½	10	620	12	15-20	+	0	±	+	0	0	Cardiac failure; cor pulmonale.
2	58	M	16	3	½	520	12	22	+	0	+	0	0	±	Cardiac failure; cor pulmonale.
3	60	M	12	?	2	420	7-10	12	++	0	+	+	0	+	Cardiac failure; cor pulmonale.
4	51	M	6	2½	1½	400	10	15	+	0	±	+	+	0	Cardiac failure; cor pulmonale.
5	50	F	18			340	3	8	+	0	±	+	0	0	Cardiac failure
6	73	M	6			200	5	14	++	0	0	0	0	0	General peritonitis
7	72	M	20			250	6	18	++	0	0	+	0	0	Bronchopneumonia
8	62	M	42			340	7	15	+	0	0	0	0	0	Cancer of colon
9	72	M	Many			520	10	25	++++	+	+	0	0	+	Cerebral hemorrhage
10	46	M	20			390	8	17	+	0	+	0	0	0	Penetrating ulcer of colon
11	60	F	8			420	4	12	++	0	0	0	0	0	Hypernephroma
12	60	M	28			360	4	14	++	0	++	0	0	0	Bronchopneumonia; asthma.
13	46	M	3			250	6	16	++	0	+	++	+	0	Pneumothorax, asthma.
14	60	M	2			340	4	22	+	0	+++	+++	0	0	Asthma
15	52	M	¾			300	7	16	+	0	+	0	+	0	Bronchiectatic abscesses; asthma.

*+ = smooth intima of major coronary vessels; ++ = numerous atheromatous plaques but no narrowing; +++ = definite narrowing of the major vessels, and ++++ = one or more major vessels occluded.

cases is shown in Table 1. Three patients had had bronchial asthma for a period of three years or less, the remaining 12 for six years or longer. Five of the latter died in congestive failure (Cases 1-5), and 4 of these showed predominant hypertrophy of the right ventricle. These 5 patients with congestive failure showed no evidence of valvular disease. The coronary arteries revealed no points of narrowing or occlusion, and the myocardium no areas of fibrosis or infarction.

Six patients (Cases 6-11) died of intercurrent diseases. In 3 of these (Cases 6-8) the heart was normal; 1 patient (Case 9) had hypertensive and arteriosclerotic heart disease, and 2 (Cases 10 and 11) showed an unexplained increase in heart weight. Asthmatic paroxysms played a prominent part in the terminal state in 4 patients (Cases 12-15), and 1 of these showed a slightly dilated right ventricle.

CASE REPORTS

CASE 1. A 53-year-old man was admitted to the hospital on July 11, 1933, complaining of a productive cough, shortness of breath, nocturnal dyspnea and edema. Twelve

*Axis deviation was determined by the angle method: angle below 0° = left axis; angle above 90° = right axis; angle 80 to 90° = tendency to right axis.

gland. The chest was barrel shaped and hyperresonant, and expiration was prolonged. There were numerous rhonchi throughout both lung fields and occasional rales at the bases. The heart sounds were slow and regular, and there was a systolic murmur at the apex. The liver edge was palpable 4 cm. below the costal margin. The blood pressure was 100/55. Roentgen examination showed a transverse cardiac diameter of 18.3 cm. and a chest diameter of 32.2 cm. The laboratory findings were normal except for a white-cell count of 14,200. The basal metabolic rate was +54 per cent on admission, but a subsequent determination was +16 per cent. It was assumed that the patient was suffering from congestive heart failure, probably due to coronary heart disease. A diagnosis of cor pulmonale secondary to bronchial asthma and emphysema was not made.

Total ablation of the thyroid gland was considered with the hope of relieving the cardiorespiratory symptoms. At operation the thyroid gland was found to be considerably enlarged. Early in the postoperative course the temperature rose and the respiratory distress became more marked. In spite of all therapeutic measures, the patient died on August 3.

The surgically removed thyroid gland, although enlarged, showed normal tissue on microscopic examination. There was no evidence of hyperplasia.

Autopsy (No. 33-70). Throughout both lung fields there were many small bronchiectatic abscesses and areas of emphysema. In the upper portion of the left lung there was a particularly large area of emphysema that com-

municated with areas deeper in the lung tissue. Microscopic examination showed extensive fibrous thickening and round cell infiltration of the alveolar septum. The heart weighed 620 gm. The right auricle was tremendously dilated. The wall of the right ventricle measured 1.2 cm and that of the left 1.5 to 2.0 cm in thickness. The coronary arteries showed no atherosclerosis and were patent throughout. There was no fibrin or evidence of infarction.

Case 2 A 58-year-old man was admitted to the hospital on October 21, 1935, complaining of cough, shortness of breath and swelling of the legs. Cough had been present for many years. Three years before admission he began to have paroxysmal attacks of shortness of breath with wheezing, which became progressively more frequent and severe. Two months before admission he noticed palpitation and orthopnea, and 6 weeks later edema of the legs appeared for the first time.

Physical examination on admission showed cyanosis, dyspnea and orthopnea. The chest was emphysematous and there were dullness and coarse rales at both bases. The heart sounds were distant and rapid but regular. The second pulmonary sound was accentuated. There was pitting edema of the lower legs and over the sacrum. The blood pressure was 120/110. The laboratory findings were within normal limits. A diagnosis of congestive failure probably due to arteriosclerotic heart disease was made.

The patient was immediately placed in an oxygen tent digitized and given sedatives. He did not respond to treatment, however, and died the next morning.

Autopsy (No. 35-92) The left lung weighed 500 gm, the right lung 640 gm. Gross sections through the right lower and middle and left lower lobes showed small subpleural areas, 2 to 6 cm in diameter, full of mucopurulent material. Microscopic examination showed dilatation of the small bronchioles and desquamation of the lining epithelium. Surrounding these small bronchioles there was much fibrosis and round-cell infiltration. The heart weighed 520 gm. The myocardium showed no evidence of softening, fibrosis or infarction. The coronary vessels were patent throughout, and their internal surfaces showed only a few small scattered atheromatous plaques. The wall of the right ventricle measured 1.2 cm and that of the left 2.2 cm in thickness.

Case 3 A 60-year-old man was admitted to the hospital on August 24, 1937, because of marked weakness, precordial pain on exertion increasing dyspnea, and peripheral edema of 9 weeks' duration. He had had attacks of bronchial asthma for 12 years, and for many years before this a nonproductive cough. Seven years before admission he had an attack of hemoptysis, for which he was admitted to a sanatorium. Six months later he was seen in the outpatient Allergy Clinic for cough and wheezing. Physical examination at that time showed cyanosis, prolonged and labored expiration, rhonchi throughout both lung fields and crackling rales at both apices. The heart action was slow and regular, and the sounds normal. There were no murmurs. The vital capacity was 1800 cc. Skin tests were positive for house dust. During the next 6½ years the patient was followed in the Allergy Clinic, but in spite of treatment, cough and wheezing continued. Approximately 2 months before admission, dyspnea and weakness became more marked and for the first time swelling of the lower extremities appeared.

Physical examination on admission showed orthopnea, dyspnea and cyanosis. Both lung fields were filled with musical and moist rales. In the right chest, below the axilla, there were amphoric breathing and cavernous crackles. The heart sounds were rapid but regular, there were no murmurs. The blood pressure was 106/68. The liver edge was felt two fingerbreadths below the right costal margin. There was marked pitting edema of both lower extremities to a point below the knees. The white cell count was 23,000, and the blood nonprotein nitrogen 33 mg per 100 cc. An electrocardiogram showed right axis deviation.

In spite of digitalization and an oxygen tent, dyspnea, orthopnea and cyanosis became progressively more marked and death occurred on the 3rd hospital day, following complete circulatory collapse.

Autopsy (No. 37-93) The right lung weighed 710 gm and the left lung 560 gm. The apical surfaces were covered with thick plaques of fibrous tissue. The bronchioles were dilated and ended in saccular dilatations filled with purulent material. Microscopic sections showed a picture of old fibrosis, newly proliferating fibrous tissue and bronchiectatic cavities. The heart weighed 420 gm. The right ventricle appeared to be hypertrophied. The coronary arteries showed a few arteriosclerotic plaques, which did not greatly narrow the lumen. There were no areas of marked fibrosis or infarction. The wall of the right ventricle measured 0.7 to 1.0 cm and that of the left 1.2 cm in thickness.

Case 4 A 51-year-old man was admitted to the hospital on February 20, 1931, because of progressive edema of the lower extremities of 6 weeks duration. Approximately 8 years previously he began to have a chronic cough, which was later associated with wheezing and attacks of asthma. This condition grew gradually worse and was more marked in the fall and winter months. His father who died at the age of 60, had had bronchial asthma. One and a half years before admission the patient was seen in the outpatient Allergy Clinic. At that time physical examination showed cyanosis, expiratory difficulty, a barrel shaped, emphysematous chest and bilateral rhonchi throughout both lung fields. The vital capacity was 1500 cc. The heart sounds were slow and regular. The blood pressure was 120/90. Skin tests were positive for several common inhalants. During the next 18 months the patient was seen in the Allergy Clinic at weekly intervals. In spite of treatment he grew steadily worse, and was therefore admitted to the hospital.

Physical examination on admission showed dyspnea and marked cyanosis, the fingertips showed clubbing, the chest was emphysematous, expiration was difficult and markedly prolonged, and there were rhonchi throughout both lung fields. The heart sounds were slow, regular and of good quality. There were no significant murmurs. The blood pressure was 125/85. The liver edge was felt three fingerbreadths below the costal margin. The legs, thighs and scrotum were markedly edematous. Stereocentigenographic examination showed no significant change in the lung fields. The transverse diameter of the heart, however, was markedly increased. An electrocardiogram showed marked right axis deviation (angle 130°). All the laboratory findings were normal except for a white cell count of 13,200. A diagnosis of congestive failure was made, but the presence of cor pulmonale due to bronchial asthma and emphysema was not suspected.

In spite of treatment, the patient showed no signs of improvement, and on the 5th hospital day he was found

in a state of collapse. Examination of the chest showed signs of consolidation in both lung bases posteriorly. He was placed in an oxygen tent. The temperature rose progressively to 104.0°F., tracheal rales developed, and the patient died on the 9th day after admission.

Autopsy (No. 31-20). There was a small amount of fluid in both pleural cavities. The lungs showed bilateral bronchiectasis with multiple bronchiectatic abscesses. The right lung weighed 1200 gm. and the left lung 590 gm. The right side of the right lower lobe was very firm, and on section this area showed a necrotic hemorrhagic abscess, 4 cm. in diameter and lined by a definite wall. The middle and upper lobes showed smaller but similar purulent areas. The left lung was somewhat collapsed. Throughout the various cut surfaces, especially in the lower lobe, grayish-white, firm raised areas were to be seen. The main bronchioles were distended and increased, and their thickened walls were traced to the periphery. Microscopic examination showed marked fibrosis, and the alveoli were lined by thickened fibrous walls. The bronchi were dilated and filled with pus. The heart weighed 400 gm. The musculature of the right side appeared almost as thick as that of the left. The wall of the right ventricle measured 1.0 cm. and that of the left 1.5 cm. in thickness. The interventricular septum showed no bulge to the right side. The coronary arteries showed no arteriosclerosis. There was no fibrosis or evidence of infarction.

DISCUSSION

The effects of bronchial asthma and pulmonary emphysema on the right side of the heart are difficult to estimate clinically. Before congestive failure has occurred, hypertrophy of the right ventricle is usually not sufficiently marked to make itself evident by x-ray study. On the other hand, when congestive failure is present, the burden of proof is on those who maintain that the bronchial asthma or emphysema is of etiologic importance. Valvular, hypertensive and coronary disease must first be excluded, and to do this autopsy data must be available. The usual method of estimating ventricular hypertrophy by the thickness of the ventricular walls is at best crude, and it is probable that minor degrees of right-ventricular hypertrophy are not infrequently overlooked. This is particularly apt to be the case when heart disease is not the cause of death and the total heart weight is near the upper limits of normal. On the other hand, when at autopsy it is noted that the right ventricle is grossly hypertrophied and the thickness of its wall is well above the usual limits of normal, it is probable that right-ventricular strain of considerable magnitude had been present.

It is significant that many of the autopsied cases of bronchial asthma reported in the literature reveal unmistakable evidence of predominant hypertrophy of the right ventricle. Thus, of 5 autopsied cases with cardiac data reported by Huber and Koessler,¹⁰ 2 had hypertrophy of the right ventricle. Harkavy¹¹ reported autopsy findings in 2 cases. One of these with bronchial asthma of only

six months' duration did not show any cardiac abnormality. The second patient, however, a woman of thirty-four, who had had bronchial asthma for nine years, died of cor pulmonale. Five years before death she began to show progressive edema which reached enormous proportions. At autopsy the heart weighed 525 gm. The right ventricle and auricle were tremendously dilated and somewhat hypertrophied. The left ventricle was normal in size. Rackemann¹² reported a case of fatal asthma in a woman of forty-three with a history of asthma of twelve years' duration. At autopsy the heart weighed 290 gm., but the right ventricle was acutely dilated. MacDonald¹³ reported cardiac findings in 8 autopsied cases. Three showed definite evidence of hypertrophy and in the remaining cases the right ventricle was dilated. Colton and Ziskin⁴ reported autopsy data in 6 cases, and of these 1 showed marked hypertrophy and dilatation of the right ventricle. Sprague⁶ reported 2 cases of fatal asthma with right-sided hypertrophy. Thieme and Sheldon³ recorded cardiac weights and measurements of the thickness of the right and left ventricles in 7 of their autopsied cases. The asthma was of short duration (one or two years) in 3 of these patients. One of the remaining 4 with asthma of long duration showed definite hypertrophy of the right ventricle.

Recently, Kountz, Alexander and Prinzmetal¹⁵ determined the weight of each ventricle separately in 17 cases of pulmonary emphysema. Since the end result of severe bronchial asthma is pulmonary emphysema, their data are germane to this problem. The cardiac findings were within normal limits in 7 cases. The remaining 10 showed predominant hypertrophy of the right ventricle. These authors reproduced similar cardiac findings in 19 dogs after the production of pulmonary emphysema experimentally. Eleven animals showed dilatation and predominant hypertrophy of the right ventricle.

The duration of bronchial asthma in 3 of our 15 autopsied cases was three years or less; the hearts were normal. In the 12 other cases, in which asthma had existed for six years or longer, 4 patients (33 per cent) showed unmistakable effects of right-ventricular strain and died in congestive heart failure. Heart failure may have been related to asthma in 1 other patient (Case 5), who showed no obvious hypertrophy of the right ventricle. Injection dissection studies by the Schlesinger technic¹⁴ in this case revealed no evidence of coronary disease. The electrocardiogram showed right-axis deviation.

Although our group of 54 cases studied only clinically showed with one exception no evidence of heart failure, the electrocardiographic examina-

tion revealed many abnormalities that can probably be ascribed to myocardial disease. This finding is in accord with the studies of Unger,¹⁵ Kahn,¹⁶ Anthony¹⁷ and Colton and Ziskin.⁴ The most significant finding was right-axis deviation in 13 per cent of the cases (angle above 90°). In another 9 per cent, a tendency to right-axis deviation was present (angle 80 to 90°). This is particularly significant, for it has been shown that right-axis deviation producing an angle of 90° or over is regularly associated with predominant hypertrophy of the right ventricle. In a series of 68 normal hearts, for example, Proger and Davis¹⁸ did not find a single case with an electrical axis above 80°. Of the patients in whom asthma was present for ten years or longer, the incidence of right-axis deviation was 18 per cent. Apparently, the longer the duration of asthma, other factors being equal, the greater the strain on the right ventricle and the higher the incidence of right-axis deviation. Right-axis deviation of the magnitude noted cannot be accounted for by alteration in the position of the heart due to a low diaphragm. These changes in the electrocardiogram are in harmony with the occurrence of right-ventricular hypertrophy at autopsy.

It would appear, then, that cardiac complications in the course of bronchial asthma and its sequelae, emphysema and bronchiectasis, are much commoner than is generally believed. When circulatory failure first appears, its diagnosis is often made difficult by dyspnea of emphysematous origin. Although some patients with cor pulmonale show edema for many months before death, others do not. In Case 2, for example, there was progressive dyspnea for three years. Peripheral edema and pulmonary congestion, however, were present for only a few weeks before death. Also in Cases 3 and 4 the presence of edema before death was of short duration. Thus, rapidly progressing heart failure may appear suddenly in patients with cor pulmonale.

SUMMARY AND CONCLUSIONS

The heart was studied in 69 patients with bronchial asthma; the autopsy findings in 15 of these cases are analyzed.

Electrocardiographic abnormalities, indicating right-ventricular strain and myocardial damage, were noted in a comparatively high percentage of patients with chronic bronchial asthma.

Five of 12 autopsied cases with bronchial asthma of six or more years' duration died in congestive failure, and 4 of these showed predominant hypertrophy of the right ventricle.

Cor pulmonale due to chronic bronchial asthma is a commoner disorder than is generally recognized.

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A DIETARY STUDY OF SUBJECTS FROM UPPER INCOME GROUPS*

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THIS dietary study was undertaken in 1940 because so little has been done on the dietary pattern of private patients. We decided, therefore, to analyze the diets of private patients to determine their daily intake of dietary essentials. We also considered it worth while and interesting to record the number of adults, from the same income level, but not under active medical supervision, who daily consumed the foods that the Committee on Foods and Nutrition of the National Research Council has stated every person must have to secure the required amounts of dietary essentials.

MATERIAL AND METHODS

Two hundred and twenty-five patients, 92 males (9 of whom were physicians) and 133 females, of various ages, from the upper income brackets and representing a cross-section of private patients attending our clinic, were selected for this study. In addition, 223 persons (20 of whom were physicians), from various upper-middle-class groups that we addressed from time to time, answered questionnaires regarding their dietary pattern; they were not, so far as we knew, under medical supervision.

For each of the 225 patients, we had a complete dietary history, including food habits, dislikes, intolerances and cravings, and a seven-day dietary calculation formulated on the basis of a diet questionnaire filled out by each patient—including the amounts and kinds of all food and liquid ingested, both during and between meals, and the mode of preparation of food. The patients were given these questionnaires when they first presented themselves with their complaints, and were told to fill them out meal by meal for a week, expressing quantities in cupfuls, tablespoonfuls, teaspoonfuls, ounces or number of units, such as one tomato, half a tomato and so forth. When they returned a week later with their questionnaires filled out, we went over them with the patients, making certain that salad dressings, sugar and cream, and the like were recorded. While reviewing their diets, we also suggested dietary changes in line with their specific ailments.

Since exact weights of the amounts of food con-

sumed were not recorded, we realize that our findings may not have been completely accurate. However, we are of the opinion that, had we asked the patients to weigh their food, we should have had little co-operation. Furthermore, although the amounts recorded were not completely accurate, we believe that we have a true picture of the patients' dietary patterns and that in these patterns dietary deficiencies were evident. Whether a diet contained 3800 or 4000 international units of vitamin A made little difference, the important fact being that the diet was deficient in vitamin A.

The diets were calculated to determine the amounts of protein, fat, carbohydrate, calories, vitamins A, B₁, B₆ and D, ascorbic acid, riboflavin, niacin, calcium, phosphorus, iron, copper, potassium, sulfur, magnesium, manganese, sodium, chlorine, acid-base, fiber and water. The food values were obtained chiefly from Bowes and Church's *Food Values of Portions Commonly Served*, both the third and the fourth edition.¹ While we were still in the process of calculating diets, Bowes and Church published the fourth edition of their book and we proceeded to make our calculations from this edition. In addition to Bowes and Church's text, we used Hawley and Maurer-Mast's.² We modified many of Bowes and Church's figures in their third edition in accordance with Munsell's³ work, and went to the original literature^{4, 5} for calculations on the trace minerals. Unfortunately, our data for the trace minerals and for niacin and vitamin B₆ were not complete because of lack of information on their content in many foods. While we were using Bowes and Church's third edition, we expressed vitamin B₁ and riboflavin in terms of international units and Sherman-Bourquin units respectively; when we went to their fourth edition, we used their revised method of expression—vitamin B₁ and riboflavin in micrograms.

After the patients' diets were calculated for their weekly intakes, we divided by 7, to determine the average daily intakes. We did not calculate daily intake of trace minerals, vitamin B₆ and niacin, since our data were incomplete; we merely computed the weekly intake of these factors. The diets were then scored for each of the dietary essentials—protein, calories, vitamins A and B₁, riboflavin, ascorbic acid, calcium, phosphorus and iron—on the basis of the standards set up by the Committee on Foods and Nutrition of the National

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Research Council,¹ taking into consideration age, sex and activity (Table 1). These are tentative allowances and can be met by a good diet of natural foods, which will also provide other minerals and vitamins whose requirements are less well known.

A deviation of 5 per cent was allowed for all the essentials except calories, for which we allowed 10

tively and if the amount recorded was "little," as 4 gm respectively. Since we could not calculate the amount of vitamin D derived from sunshine, we merely recorded the amount of vitamin D in the weekly diet.

We then accumulated our data on these 225 diets to determine how many were deficient in vitamin A, how many were deficient in vitamin

TABLE 1. Recommended Allowance for Specific Nutrients²

	ENERGY	PROTEIN	CALCIUM	IRON	VITAMIN A*	THIAMINE (VITAMIN B ₁)†	RIBOFLAVIN	NIACOTINIC ACID	VITAMIN C (ASCORBIC ACID)	VITAMIN D
	cal	gms	gm	mg	int. units	mg	mg	mg	mg	int. units
Man (70 kg)										
Moderately active	3000	0	0.8	12	5000	1.8	2.7	18	5	
Very active	4500					2.3	3.3	23		
Sedentary	2500					1.5	2.2	15		
Woman (56 kg)										
Moderately active	2500	60	0.8	12	5000	1.5	2.2	15	70	
Very active	3000					1.8	2.7	18		
Sedentary	2100					1.2	1.8	12		
Pregnant (latter half)	2500	85	1.5	15	6000	1.8	2.5	18	100	400-600
Lactating	3000	100	2.0	15	6000	2.3	3.0	23	150	400-600
Children up to 12 years										
Under 1 year‡	1000/kg	3-4/kg	1.0	6	1500	0.4	0.6	4	30	400-600
1-3 years§	1200	40	1.0	7	2000	0.6	0.9	6	35	
4-6 years	1600	50	1.0	8	2500	0.8	1.2	8	50	
7-9 years	2000	60	1.0	10	3500	1.0	1.5	10	60	
10-12 years	2500	80	1.0	12	4500	1.2	1.8	12	75	
Children over 12 years										
Girls										
13-15 years	2800	85	1.3	15	5000	1.4	2.0	14	80	
16-20 years	2400	5	1.0	15	5000	1.2	1.8	12	85	
Boys										
13-15 years	3200	85	1.4	15	5000	1.6	2.4	16	90	
16-20 years	3800	100	1.4	15	6000	2.0	3.0	20	100	

*Requirements may be less if provided as vitamin A₁ or if provided chiefly as the provitamin carotene.

†1 mg thiamine = 333 int. units. 1 mg ascorbic acid = 10 int. units.

‡Needs of infants increase from month to month; the amounts given are for approximately 6 to 8 months. The amounts of protein and calcium needed are less if derived from breast milk.

§Allowances are based on needs for the middle year of each group (7, 8, 9 and so forth) and for moderately active.

¶Vitamin D is undoubtedly necessary for older children and adults; when not available from sunshine it should be provided probably in minimum amounts recommended for infants.

per cent. We established the following standards for the other constituents of the diet in line with scientific research: carbohydrate, 50 to 60 per cent of the total calories⁷; fat, 20 to 35 per cent of the total calories⁸; acid base, both the same or slightly more acid than base⁹; fiber, 50 to 63 gm¹⁰; and water, 2800 cc¹¹. For carbohydrate and fat, we allowed a 5 per cent, and for fiber and water, a 10 per cent deviation. Since our data were incomplete for the trace minerals, vitamin B₁ and iron, we did not score the diets on these components. Regarding sodium and chlorine, we questioned the patient concerning the amount of salt used. If the amount was stated as "average," we estimated the salt intake, in addition to the amount found in food, as 6 gm of sodium and 6 gm of chlorine daily; if the amount was "large," we estimated the daily sodium and chlorine as 8 gm respec-

tively and so forth, and to determine their degree of deficit. For the trace minerals, vitamin B₁, iron and vitamin D, we expressed our findings in terms of numerical ranges.

We also recorded how many diets had only one deficiency, how many had two deficiencies and so forth. In accumulating these data, we considered only protein, calories, calcium, phosphorus, iron, vitamins A and B₁, ascorbic acid and riboflavin, since these are the dietary factors that are principally concerned. We have eliminated the other factors for the following reasons: fat and of calcium, because much about the ill or cent of the drate, acid whether forming

in human nutrition¹²; fiber, because individual needs and methods of cookery vary greatly and influence the requirement and the content of fiber would be deficient in vitamin B₁; if the amount of meat ingested was small, the diet would probably be deficient in riboflavin (unless a good deal

TABLE 2. Number of Cases of Dietary Imbalance in 225 Private Patients.*

TYPE OF IMBALANCE†	NO. OF CASES AND DEGREE OF IMBALANCE						TOTAL NO. OF CASES
	5-10%	10-20%	20-30%	30-40%	40-50%	+50%	
Protein deficiency	21	23	17	16	3	2	82 (36.5%)
Fat deficiency	-	-	-	-	-	-	0 (0.0%)
Fat excess	29	39	65	43	16	8	200 (88.0%)
Carbohydrate deficiency	48	72	56	15	7	2	200 (88.0%)
Carbohydrate excess	1	-	-	-	-	-	1 (0.4%)
Calorie deficiency	-	33	50	44	29	11	167 (74.0%)
Calorie excess	-	5	5	-	-	-	10 (4.4%)
Vitamin A deficiency	10	12	12	10	3	11	58 (26.0%)
Vitamin B ₁ deficiency	8	22	41	37	35	29	172 (76.0%)
Riboflavin deficiency	10	19	22	30	35	58	174 (77.0%)
Ascorbic acid deficiency	1	8	6	3	1	10	29 (13.0%)
Calcium deficiency	11	20	13	23	8	29	104 (46.0%)
Phosphorus deficiency	9	12	20	11	1	1	54 (24.0%)
Iron deficiency	14	27	26	11	10	2	90 (40.0%)
Water deficiency	-	25	41	30	39	28	163 (72.0%)
Water excess	-	-	-	-	2	1	3 (1.3%)
Fiber deficiency	-	31	27	35	26	36	155 (69.0%)
Fiber excess	-	6	4	-	-	-	10 (4.4%)

*Patients eating between meals numbered 94, or 42 per cent; this figure does not include those who ate fruit, fruit juices or milk, which do not interfere with appetite.
†In addition, 161 patients, or 71.5 per cent, had an acid-base imbalance; of these, 155 had more base-forming and 6 more acid-forming foods.

in foods; and other factors, because the data were incomplete. After analyzing over two hundred diets, we could deduce merely from looking over the weekly diets whether or not the dietary essentials were provided in adequate amounts. For example, if a of milk was consumed), phosphorus and iron; and if there were no citrus fruits or raw cabbage or green pepper or raw green leafy vegetables, the diet would be faulty in ascorbic acid. We then analyzed the dietary "yardstick" adopted during the National Nutrition Conference,¹³ and

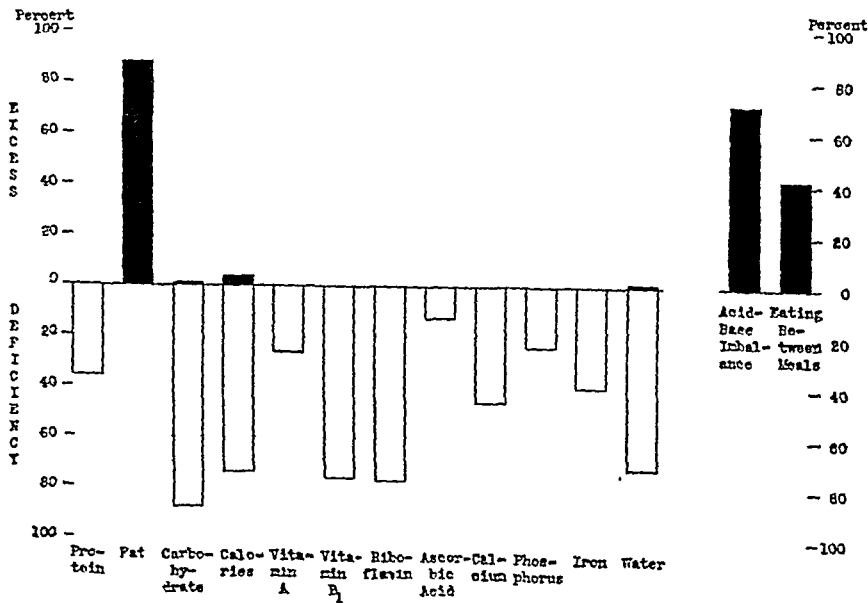


FIGURE 1. Summary of Patients' Dietary Imbalances.

pint of milk was not ingested daily, the diet would be deficient in riboflavin, and probably also in calcium, since the amount of calcium present in other sources, such as vegetables, is not adequately utilized and is variable, depending on the calcium content of the soil; if white bread was taken instead of enriched white or whole-wheat bread, the diet found that a daily consumption of at least one pint of milk, three slices of whole wheat (or enriched) bread or its equivalent in whole-grain cereal, one serving of meat, one egg, two servings of vegetables, two servings of fruits (one of which should be a citrus fruit) and two and a half tablespoonfuls of butter, cream or fortified oleomargarine,

provided the following essentials: 1500 calories, 62.2 gm. of protein, 0.85 gm. of calcium, 17.2 mg. of iron, 4300 international units of vitamin A, 1400 microgm. of Vitamin B₁, 80 mg. of ascorbic acid, and 1700 microgm. of riboflavin. A comparison with the standards reproduced in Table 1 indicates how many of the dietary essentials are furnished by this dietary yardstick, which supplies less food than the average person ingests.

We then decided that it would be worth while to compare the diets of patients and healthy persons, to obtain a picture of the dietary deficiencies of the upper income groups. We therefore distributed questionnaires to members of lay and professional groups whom we addressed from time to time, asking them to record "yes" or "no" to questions concerning their daily ingestion of the foods listed in the dietary yardstick. The answers to these queries were recorded and compared with the dietary pattern of the patients.

DIETARY FINDINGS IN PRIVATE PATIENTS

The dietary computation in 225 private patients is shown in Table 2.

Figure 1 illustrates graphically the percentage range of these dietary deficiencies and faulty habits. The values for other factors are expressed in numerical ranges on a weekly basis (Table 3). Although little is known of the functions in the body of the trace minerals and vitamin B₆, clinical evaluation of such factors will undoubtedly be accomplished in the future, and perhaps, these ranges will be of value to other investigators. However, it is known that manganese is necessary for the synthesis of vitamin B₁ and ascorbic acid, that a deficiency of copper may produce anemia, and that excess fluorine causes dental caries.

It should be noted that the diets of the majority of patients were high in fat (Fig. 1). We believe this excess is linked with large amounts of money to spend for food, since butter, cream, creamed vegetables, rich desserts and the like are relatively expensive. We have found that persons in the lower income levels cannot afford to spend large amounts of money on fat, and as a result their diets are significantly lower in fat.

Diets of Physicians

Among the 225 patients were 9 physicians whose diets were as bad as those of the other patients. Two of the 9 were deficient in protein; all had an excess of fat; all were deficient in carbohydrates; 7 were deficient in calories; 4 were deficient in vitamin A; all were deficient in vitamin B₁; 8 were deficient in riboflavin; 1 was deficient in ascorbic acid; 4 were deficient in calcium; 1 was deficient in phosphorus; 5 were deficient in iron;

4 had acid-base imbalance; 7 were deficient in water; and 3 ate between meals.

Preparation of Food

According to the patients' answers to questions regarding vegetable cooking, in most cases the veg-

TABLE 3. Other Factors in Diets of 225 Private Patients.

Factor	Amount		No. of Weekly Diets
	int. units mg.	gm.	
Vitamin B ₆	0-1750		43
	1750-3500		62
	3500-5250		52
	5250-7000		36
	Over 7000		32
Niacin	0-35		174
	35-70		31
	Over 70		20
Vitamin D	0-175		40
	175-350		164
	350-525		60
	525-700		11
	Over 700		10
Copper	0-5		76
	5-10		118
	10-15		23
	15-20		6
	Over 20		2
Potassium	0-5		20
	5-10		78
	10-15		85
	15-20		29
	Over 20		13
Magnesium	0-1		115
	1-2		99
	2-3		11
Manganese	0-5		48
	5-10		91
	10-15		45
	15-20		25
	Over 20		16
Sodium*	Below 30		2
	30-40		29
	40-50		132
	50-60		46
	Over 60		16
Chlorine*	Below 30		1
	30-40		21
	40-50		71
	50-60		111
	Over 60		21

*Includes amount used in table salt.

etables were not prepared or cooked properly. A good deal of water was used in cooking, the remaining pot liquor was not used, potatoes were not cooked in their jackets and so forth. Therefore, in most cases, because of losses in cooking, the diets of the patients undoubtedly contained less vitamins and minerals than were found on calculation.

Multiplicity of Dietary Deficiencies

It must be remembered that vitamin deficiencies are multiple and are rarely found alone, not only because a diet that is deficient in one factor is usually deficient in more than one factor, but also because a deficiency of one factor causes a greater strain on the other factors and, in turn, brings about an increase in the body's demand for these.

On compiling the data concerning the number of diets that were deficient in one or more of the essential factors,—protein, calories, vitamins A and B₁, ascorbic acid, riboflavin, calcium, phosphorus and iron,—we found the following: diets deficient in 0 factors, 28, or 12 per cent; diets deficient in 1 factor, 21, or 9 per cent (1 physician);

that at the time this survey was made only a small fraction of the white bread sold on the market was enriched. Yet the figures concerning the general consumption of whole wheat or enriched bread belie this statement. We are certain that the non-medical subjects of our survey often answered "yes" to many questions in the questionnaire be-

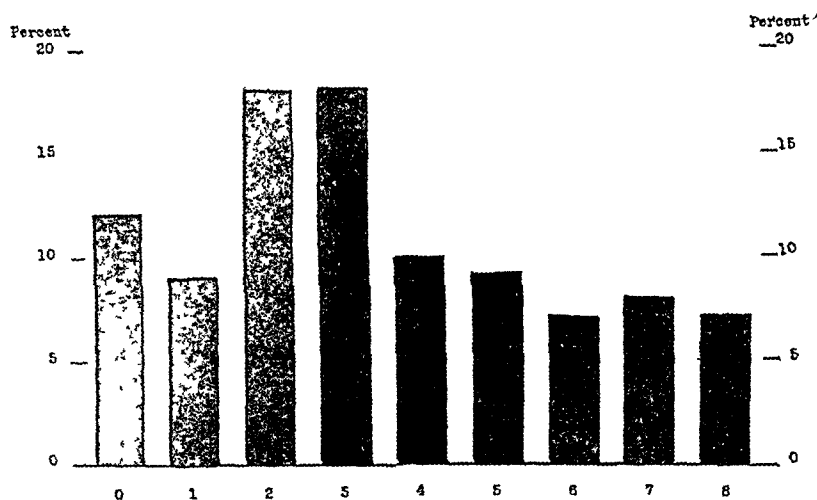


FIGURE 2 Incidence of Number of Essentials in Which Patients' Diets Were Deficient

diets deficient in 2 factors, 42, or 18 per cent; diets deficient in 3 factors, 41, or 18 per cent (4 physicians); diets deficient in 4 factors, 23, or 10 per cent (2 physicians); diets deficient in 5 factors, 21, or 9 per cent; diets deficient in 6 factors, 16, or 7 per cent; diets deficient in 7 factors, 18, or 8 per cent (2 physicians); and diets deficient in all factors, 15, or 7 per cent.

Of the 21 diets deficient in 1 factor, 9 were deficient in vitamin B₁, and 8 in riboflavin; of the 42 diets deficient in 2 factors, 36 were deficient in both B₁ and riboflavin (Fig. 2).

DIETARY FINDINGS IN PRESUMABLY HEALTHY PERSONS

We endeavored to determine how closely the dietary pattern of our group of 225 private patients conformed with that of a group of 223 non-medical subjects of similar socioeconomic status. To accomplish this, we recorded the answers of the "nonpatients" to a series of questions concerning their daily ingestion, in proper amounts, of the foods listed in the dietary yardstick.¹³ The data thus obtained are presented in Figure 3.

In a survey of this sort, many errors are incurred. For example, we are convinced that not many people eat whole-wheat or enriched bread. This has been proved by the calculation of the diets of our patients and also by the fact that the consumption of whole-wheat bread is very small and

cause they knew the answer should be "yes." However, for purposes of comparison, we found these questionnaires valuable.

DISCUSSION

In this study we observed that more of the diets of the private patients were deficient in vitamin B₁ and riboflavin than in any of the other vitamins or minerals. A recheck of the foods eaten or not eaten revealed that daily quotas of milk (one pint), whole-wheat or enriched grain products (two or three slices of bread or its equivalent in cereal), eggs (three to five a week) and fruit (two servings) were supplied by the diet *less often* than those of other nutritionally essential foods were.

Since the diets were often low in milk, they were of necessity low in riboflavin (and also calcium), and being low in whole-wheat or enriched grain products, they were low in vitamin B₁. The lack of eggs is not clearly illustrated by a definite deficiency in the diet, for the various minerals and vitamins contained in eggs can be supplied by other foods. In most cases, one serving of fruit was consumed daily. The lack of a second serving did not result in a specific dietary inadequacy, since the large consumption of vegetables made up for this lack. Because the consumption of fat, citrus fruits and vegetables was high, there were but few deficiencies in vitamin A and ascorbic acid. Since the protein intake in

many cases was low, iron and phosphorus deficiencies appeared.

A comparison of the patients' diets with the diets of nonpatients indicated that the dietary

70 disliked milk; and of 206 with euclorhydria (normal hydrochloric acid content), 40 disliked milk. However, we believe that some still undetermined condition in the large number of people

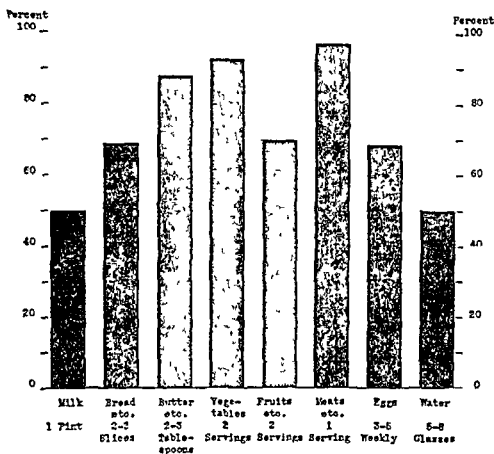


FIGURE 5 Summary of Nonpatients' Daily Dietary Pattern

pattern of the latter was about the same as that of the former. In the questionnaires returned by the nonpatients, there were more "no" answers to queries concerning adequate consumption of milk, eggs, fruit and whole-wheat or enriched grain products than to those concerning the other essential foods. The water intake was low in both groups. If these diets could be calculated quantitatively, deficiencies of riboflavin and vitamin B₁ undoubtedly would rank highest. Most of the nonpatients obtained their one serving of meat daily, but only one serving of meat each day does not satisfy the protein requirement because the milk and, possibly, the eggs are needed to supply the balance.

After questioning patients and nonpatients, we found that there were many reasons why people did not drink milk. Milk was considered fattening, milk made them constipated, milk gave them indigestion and so forth. We believed that some somatic condition caused an intolerance to milk and thought that this intolerance might be linked with a condition of achlorhydria. We therefore made a survey of 597 patients who attended this clinic, checking the patients' dislike for milk and the hydrochloric acid content of their gastric juices. Unfortunately, there seemed to be no correlation. Of 80 patients who had histamine achlorhydria, only 20 disliked milk; of 311 with hypochlorhydria,

who dislike or do not tolerate milk is correlated with such intolerance.

SUMMARY AND CONCLUSIONS

The diets of 225 private patients from the upper income level, 9 of whom were physicians, were calculated.

Questionnaires regarding dietary pattern were filled out by 223 persons from the upper income level, 20 of whom were physicians, but none of whom were under direct medical supervision.

Among the private patients, the most prominent dietary deficiencies were in vitamin B₁ and riboflavin—76 per cent of the patients being deficient in vitamin B₁ and 77 per cent deficient in riboflavin.

Among those subjects not under direct medical supervision, milk, eggs, fruit and whole wheat or enriched grain products were the foods most frequently found lacking. This dietary pattern was similar to that of the patients, and on calculation, the diets of these 223 individuals would undoubtedly also be shown to be primarily deficient in vitamin B₁ and riboflavin.

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THE TREATMENT OF COMMON SKIN DISEASES*

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THE skin conditions that we see most commonly at the Vanderbilt Clinic and on the wards of the Presbyterian Hospital are acne, psoriasis, dry chapped skin, coccal infections, fungus infections and allergic dermatoses.

The first step in the treatment is the diagnosis. In addition to the appearance of lesions, there are three factors of distinct diagnostic help: the patient's story—of particular importance in the allergic group; laboratory tests, such as the direct examination of the involved skin for fungi or cocci and the use of skin tests in the diagnosis of the allergic group; and the therapeutic test, that is, specific treatment for the most likely diagnosis.

ACNE

A very mild acne is almost normal with the onset of puberty. Mild to moderately severe acne can be well treated by the general practitioner, but severe cystic and nodular acne requires the specialist's care. The treatment may be divided into local and systemic. Local care includes meticulous and prolonged work. At bedtime the areas involved should be thoroughly scrubbed with either tincture of green soap or sulfur soap. The comedones should be expressed with a blackhead remover and then sulfur—either Lalotin (Lascoff) or Sulpholac (Alba)—should be massaged into the areas in which the blackheads have been removed. In the morning the sulfur is removed by thorough scrubbing with warm water and soap. This is followed by rinsing with cold water. Powder may be used, but all creams and greases should be avoided. The systemic treatment of acne should include normal adequate caloric intake and the avoidance of chocolate, iodine, and an excess of sweets and greasy foods; a unit of exercise; and protection from direct sunlight and the use of a system of protection, such as

constipation or dysmenorrhea. The discrete use of endocrine preparations in patients having clear-cut menstrual difficulties is worthy of trial.

PSORIASIS

As in the treatment of acne, the therapy of psoriasis resolves itself into local and systemic. Dermatologists no longer believe that the patient with psoriasis need go about feeling that nothing can be done for him. Much can be done with purely local therapy, such as crude coal tar and the ultraviolet treatment of Goeckerman.¹ However, there is an increasing literature suggesting that psoriasis is a disturbance of lipid metabolism. Since 1933 a number of reports have appeared in the German literature on the successful treatment of psoriasis by rigid adherence to a diet not exceeding 20 gm. of fat daily. Later Dragstedt and his co-workers² reported that 17 out of 23 patients became free from psoriasis following the ingestion of lipocaic. This lipotropic substance, which is isolated from the pancreas, prevents or cures the fatty liver that develops in depancreatized dogs maintained on insulin. Since 1939 we have been trying various lipotropic substances, such as crude liver, rice polish, yeast concentrate, soy-bean phosphatides and defatted wheat germ, in the treatment of psoriasis. With the use of the last two we have had astonishingly good results, particularly in the early type of lesions. The soy-bean phosphatide preparation that we have used is Lexo Cookies (American Lecithin Company); the patients eat from two to five of these daily. The defatted wheat germ is called Vio-Bin (Vio-Bin Corporation); one to two tablespoonfuls are eaten daily.

Along with the lipotropic substances the local medication has been one of the newer tar preparations—3 per cent Nu-kol-tar (Benet) or 5 per cent Neo-tar (Lascoff) ointment. Many dermatologists use one of the di-oxyanthralin derivatives, such as 0.1 to 0.5 per cent Anthralin (Abbott) ointment.

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Two generalizations may be made concerning the local treatment of psoriasis. In an acute outbreak only soothing applications should be used, and when the eruption is chronic the lesions should be stimulated with one of the preparations mentioned above. Furthermore, at the beginning the various medicaments should be of average or below-average strength, and the strength increased if necessary; for example, one may begin with 0.1 per cent Anthralin and progress to 0.5 per cent. The older vehicles—lanolin, benzoated lard, petrolatum and so on—are being rapidly replaced by wetting agents in water-soluble bases. In these may be incorporated most local medicaments. They are nongreasy, much more penetrating, and wash off readily. At present there are three excellent ones: Solucreme (Lascoff), Hydrosorb base (Abbott) and Mull-sol (Hickok).

DRY, CHAPPED SKIN

Dry, chapped skin is very prevalent in the winter time among people with rather thin skins, and those who wash their hands frequently, such as physicians. Sometimes in addition sharply defined patches of eczema develop on the extremities.

The skin should be treated gently. Soft water should be used if available. Mild or superfatted soaps, or the newer detergents, such as Laval (Hickok) and Terses (Doak) are to be preferred. They are less hard on the skin than the ordinary soaps. The soap should be rinsed off and the skin carefully dried, and anointed with oil or cold cream at bedtime. Vitamin A is almost a specific for very dry skin. It is well to stress foods high in vitamin A and in addition to prescribe 75,000 units of vitamin A a day for a few weeks and then reduce it gradually to 25,000 units a day for a few months.

COCCAL INFECTIONS

For staphylococcal and streptococcal infections of the skin—the commonest, perhaps, being impetigo—treatment with sulfathiazole is simple. Formerly a child with such an infection was excluded from school for weeks, but now it is possible for him to return to school within three or four days. One can use either 5 per cent sulfathiazole in a water-soluble base containing a wetting agent, or, if glycerin is available, about 8 parts of warm glycerin to 1 part of sulfathiazole. Either of these should be applied to the lesions every three or four hours.

We have not had good results with the local use of sulfonamides for boils. This is understandable because of the presence of pus.

For chronic, recurrent boils, dermatologists have a therapy different from that of surgeons or roent-

genologists. In the few cases which reach the dermatology clinic we have found staphylococcal toxoid of remarkable benefit. Its use seems logical because the patient has insufficient resistance to an organism found on the skin. An effort is made to stimulate antitoxin production. Intradermal injections of staphylococcal toxoid (Lederle) are given three times a week. The average initial dose is 0.1 cc. of a dilution containing 1000 necrotizing units per cubic centimeter. The dose is increased by 0.1 cc. each time up to 0.7 cc. Then the next stronger dilution (10,000 units) is used and the course is repeated.

With this type of therapy, the boil may come to a head or may be reabsorbed. Usually no more boils occur after the patient has had a few injections.

FUNGUS INFECTIONS

It has been suggested that the best way to cope with superficial fungus infections is to let everyone have such an infection and learn to live with it. There are two types of causative organisms; dermatophytes, affecting the skin, hair and nails; and yeastlike fungi, the monilias, affecting the skin, nails and mucous membranes.

Perhaps the most effective therapeutic agent is gentian violet. If there is a tender, excoriated or fissured area, a 2 per cent aqueous solution can be used. If not, 2 per cent gentian violet in 25 per cent alcohol is preferable. Once the lesion becomes chronic, a medicament is necessary that will cause exfoliation. Whitfield's ointment is as good as any. For a fungicidal powder, B.F.I. (Mulford), is acceptable.

Reinfection in ringworm infection is probably not very common. There is, rather, a persistent infection, the site being usually the nails of the great toes. If they are serrated, discolored, too thick or too thin, the fungus may be there, and it is well to keep on treating the nails with alcoholic gentian violet.

For the differential diagnosis, it is quite easy to obtain the fungus or the yeastlike organism on culture or to recognize it by direct slide examination. When it is a question of whether the condition is a fungus infection, contact dermatitis or something else, one should take advantage of this laboratory procedure.

With ringworm infections the stockings should be sterilized. Of course, cotton is easily sterilized, but silk or wool is not. The best thing to do is to launder the hose and press them on the wrong side with a hot iron. Shoes do not need to be sterilized if stockings are worn. Bedroom slippers

can be discarded, or sterilized by placing small open jars of formalin in them for a few hours.

ALLERGIC DERMATOSES

Drug Eruptions

Drug eruptions are becoming an increasing problem. There are about two hundred drugs in common use. Unfortunately, any drug may produce an eruption, and practically every known dermatologic condition can be produced by them. A few of them are characteristic. The diagnosis of a drug eruption is made by its sudden appearance, its symmetrical distribution, its extensiveness in comparison with the systemic disturbance, and its brightness.

The history of drug ingestion is sometimes unobtainable; however, the patient has usually been taking the drug for some time. It seems desirable to dispense with some of the drugs now in use, at least some of the sedatives. A walk around the block or a hot bath may be advised instead. The treatment consists in prohibiting the use of the drug and in allaying the itch with sodium bicarbonate baths and calamine lotion.

There are few specific treatments for drug eruptions, with the exception of bromide and iodide eruptions, for which we give sodium chloride. In persons known to be sensitive to arsphenamine, it has been possible to give vitamin C prophylactically. Even after the eruption is present, the use of vitamin C is helpful.

Allergic Eczema

Allergic eczema is commonly seen in infants. It occurs on the flush areas, over the head and neck, and it may become widespread. It may clear up or persist. When it recurs in early childhood, it has no very characteristic distribution except that it is symmetrical and patchy. In adolescence and adult life, a characteristic picture is present: it is perfectly obvious that the skin has been scratched. The eczema occurs on the face and neck and in the antecubital and popliteal creases. For these adults with persistent eczema, dermatology clinics have little to offer. But we are anxious to treat the infant or the child with an eczema that has persisted more than six months in order to determine the substances to which he is sensitive.

Allergic eczema is primarily a gastro-intestinal sensitivity and, unfortunately, the infant is usually sensitive to the foods he eats: milk, most; egg white, cow's milk, wheat, or corn; chocolate, so on.

The most helpful clue is the child's history. The physician will say that shortly after

child refused it. She insisted on it, and the rash developed. Or a mother will say, "Almost from the start, the child didn't like that, cried after eating it, had diarrhea, and then broke out." A careful history is of even more value than skin tests.

Testing the skin to common foods is of value. It is a laboratory procedure, and one must not depend on it too much. If one has the good fortune to obtain a positive skin test, it means the child is or was sensitive to that food, and such a sensitivity may be extremely significant.

Of greatest value is the use of elimination diets. They were first brought out by Rowe,³ and have been expanded and changed by investigators since that time. Thus, a child with severe eczema, on whom no testing can be done, can be placed on an almost synthetic diet. For milk, one can substitute a soy-bean preparation — Sobee (Mead-Johnson) or Mull-soy (Borden) — that is perfectly adequate. Crystalline vitamins A and D may be given, and corn meal or rice as a cereal. When the child improves on this regimen, a new food may be added at three-day intervals. As one continues with additions to the diet, there may be a recurrence of eczema. When this happens the last food added is eliminated. With painstaking care, it is quite possible to determine to which foods a child is sensitive and to eliminate them or desensitize him to them. If a patient is found to be sensitive to an important food, oral desensitization is readily accomplished.

The person with allergic eczema has the ability to become easily sensitized, and if he is not treated vigorously in early life, multiple sensitivities occur. The allergic infant with eczema, at least for the first year, is probably sensitive only to foods, and usually not to very many. After the first year, he acquires sensitivities to other foods and substances, such as wool and silk and bacteria. He is always scratching his skin so that it is chronically inflamed and the patient becomes increasingly sensitive, his sensitivity becoming an almost insurmountable barrier in adult life.

If one is carrying on a diet like the above only bland ointment is necessary. The child is given a standard diet, and a saline is applied.

If one prefers not to use the above diet, one may use a standard diet. There are many preparations of desensitizing agents.

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with normally innocuous substances. This sensitivity is not hereditary and the lesion is generally localized at onset to the exposed areas. Unfortunately, as with the drug eruptions, there is almost no substance to which the skin may not become sensitized; the commonest such substance is poison ivy.

The diagnosis of contact dermatitis is often made through the history. The use of patch or contact tests is very helpful. It is not necessary to have any elaborate setup for this type of testing. The suspected substance should not irritate the normal skin (one can put a patch on himself first, and then try it on the patient). For example, if the patient is thought to be sensitive to turpentine, one can make a 1 per cent solution of turpentine and put it on the normal skin, cover it with a piece of adhesive tape, and leave it on for twenty-four hours. If he is sensitive to it, an erythema with vesicles will appear at the test site.

The treatment depends on the stage of the eruption. If the eruption is acute, wet dressings or baths are indicated. If it is subacute, lotions or pastes are used.

It has been shown that almost anyone can become sensitive to poison ivy. Usually the person who pulls it up and says, "Nothing ever happens to me" is the one who finally gets the worst attack.

The best approach to the problem is: first, avoid poison ivy; and, second, if you come in contact with it, do something about it as soon as possible. The chances are that if the sensitizing oil is removed from the skin within four hours, one may not get an attack. The affected area should be thoroughly scrubbed with brown soap and water, rinsed well, and sponged off with alcohol.

If soap and water are not available, the ivy may be neutralized by smearing the skin with the juice of the plantain or jewel weed.

If one is susceptible to ivy and unable to avoid it, desensitization is indicated and is often very effective. It may be accomplished by either the oral or the intramuscular route. For oral desensitization the 2 per cent tincture of the poison-ivy toxin is given, beginning with 1 drop and increasing by 1 drop daily up to 1 teaspoonful. This is continued throughout the season. The intramuscular injection should be preseasonal, and usually four injections at weekly intervals suffice.

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MEDICAL PROGRESS

ABDOMINAL SURGERY

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SINCE the effects of trauma inflicted in warfare is, at the moment, uppermost in our minds, it seems appropriate that this progress report be limited to abdominal injuries. Although reports from previous wars and civilian practice have been helpful in determining the best methods of treatment in certain types of abdominal wounds, the classic one, used as a base line in recent years, is the masterful contribution by Wallace.¹ To him, we owe the careful compilation of data collected from the actual experience of the surgeons working under his direction in World War I. Many previously disputed points regarding the management of abdominal wounds were settled. In the present war, most of our information regarding

this subject has come from British sources. This is probably due largely to the breakdown in communications and lack of free exchange of journals, but there is some likelihood that political restriction on such information has played a role.²

In this "total war," we are faced not only with the problem of wounded combatants but with that of injured civilians regardless of occupation, age or sex. This type of warfare is unique in the memory of man, as are the agents of destruction used. The complete change in the character of the machines of war in the past twenty-five years has brought about new kinds of wounds along with a type of destruction of life and property hitherto unknown. Almost completely surprised and unprepared for such extensive and varied injuries, Great Britain has met the situation in a most efficient and gratifying manner. To her, we in America owe the opportunity for preparedness,

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C. Thomas Company, 1942. \$5.00).

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even though progress in this direction has, at times, seemed unbearably slow.

The most comprehensive article so far written on the types of abdominal wounds suffered by the British in the present conflict is one by Gordon-Taylor³; it was presented by him before the Clinical Congress of the American College of Surgeons in Boston (November 3-7, 1941). In the present report he will be quoted often and liberally, since he has brought to us many important details, particularly those concerning the abdominal injuries resulting from bombing. It is my purpose to stress these civilian casualties, since those of us left at home must gather information in advance of such a catastrophe; also, problems relating to the management of abdominal wounds occurring in civil practice are always important. From various reports from the war zones, and especially from the excellent military manual on abdominal injuries prepared by Storck,⁴ we can learn much to help us when dealing with civilian wounds.

Abdominal injuries can be roughly divided into two categories: those produced by blunt force and without penetration of the abdominal wall, and those produced by penetrating objects. Both types may be associated with other injuries, such as fractures, chest wounds, cranial wounds and trauma to the soft parts of the body. In the management of such casualties, one must be on the alert for multiple injuries and be ready to treat them in order of importance, or with two or three teams working at once on different regions. The need for early and adequate treatment of intra-abdominal injuries ranks second only to the control of severe hemorrhage.

Shock occurs following all forms of severe trauma. This condition is of varying degrees and usually appears early, but may occur after some hours have elapsed. Blalock⁵ classifies patients suffering from shock in two main groups: those who have bled from injured blood vessels and appear with cold extremities due to vasoconstriction, and those whose blood loss has occurred into the great veins of the body owing to vasodilatation and who may have warm extremities. Both types show restlessness, pallor, air hunger, thirst and lowered blood pressure. A rapid, thready pulse occurs in the first group. Shock is best treated by warmth, sedation with morphine and blood or plasma transfusions according to the extent of hemoconcentration. Massive hemorrhage is the only condition warranting immediate surgical intervention before shock has been effectively treated. In abdominal injuries, this preliminary condition must be handled with the greatest expedition since the time factor is of great importance.

Mulholland⁶ points out the cause of death in abdominal trauma. The mortality in a group of cases studied by him was 51 per cent. Of these victims, 43 per cent died of shock, 43 per cent of infection, and 13 per cent of hemorrhage. It appears that future efforts will do much to lower this rate, since both shock and infection are under better control than formerly. Heyd⁷ calls attention to the simple objective test of the operative state of a patient under these conditions: that is, the warmth of the body. Doubtless many cases are subjected to surgery before shock has been controlled.

NONPENETRATING WOUNDS

Nonpenetrating abdominal injuries may result from comparatively slight trauma, such as a fall while at play. Various gradations from this to very severe crushing injuries occur. A new type of injury produced by blast has appeared since civilian bombing has been recorded. This occurs when an explosion takes place in close proximity to the victim without any shell fragment's penetrating the body. Petechial hemorrhages have been described in the brain, lungs and abdominal viscera. Actual perforations of hollow viscera have been reported, as well as thromboses of large blood vessels supplying segments of intestine. Similar injuries have been reported to men in the water from nearby explosions in the sea.⁸ Most of the intra-abdominal lesions, however, are produced through considerable impact against the abdominal wall by flying or falling objects or by moving vehicles.

Fatheree⁹ has collected from the literature the fact that 60 to 78 per cent of intra-abdominal injuries by blunt force affect the solid organs. This is due to the firmer fixation of these structures as compared with the mobility of the hollow viscera. When one is confronted with the problem of intra-abdominal trauma, it is important to realize the possibility of serious injury and to classify each case as one of minor injury to the parenchymatous organs requiring no operation, a hopeless situation with multiple injuries beyond rescue, obvious injury to a hollow viscus or continued hemorrhage from solid organs or the mesentery, or a borderline case in which there is reason for doubt. Both the last-named types require surgery as soon as shock has been controlled and conditions permit. The sooner a rupture of the intestine or bladder is sutured, the greater is the likelihood of a successful outcome.

Liver injuries are of all gradations. The mild ones may be recognized by the minimal trauma and symptoms. If one could be sure that there were no other viscera involved, many exploratory

laparotomies could be avoided. Hinton¹⁰ pointed out years ago that the bleeding in liver injuries has usually ceased at the time of exploration. It has often been observed that it is unwise to disturb such a clot, and one should be content to remove the extravasated blood and bile from the abdominal cavity by means of a suction tip alone. In large rents that are still bleeding, one must either pack the area with gauze, cauterize the bleeding surfaces or attempt suture. Corriden¹¹ has reported a case of severe subcapsular rupture of the liver successfully treated by a large transplant of rectus muscle into the sulcus. Grey Turner¹² points out that the mortality in liver injury is high and states that hemorrhage accounts for 60 per cent and sepsis for 40 per cent of the deaths. He describes an ingenious method of suturing a rent in the liver. By first placing a large strand of catgut through the substance on each side of the opening parallel to the edges, he is able to prevent his deep transverse sutures, passed outside the transverse strands, from cutting out. Totten¹³ and Estes¹⁴ have called attention to digital compression of the hepatic artery and portal vein during the manipulations necessary for controlling the bleeding from the wound itself. Hawthorne, Oaks and Neese¹⁵ report an interesting case of liver injury manifesting itself by repeated massive hemorrhage through the bile ducts.

In a previous publication, I¹⁶ have cited a fatality from autotransfusion of the blood collected from the abdominal cavity in a patient with ruptured liver. This patient died of anuria, probably through the toxic action of the bile on the kidneys. Since this case was published in 1931, various authors have called attention to the danger of autotransfusion in liver injuries. The term "hepatorenal syndrome" has been used by Orr and Helwig.¹⁷ More recently McCorkle and Howard¹⁸ have reviewed the question of liver damage followed by other complications, and report a case showing transient urinary suppression following laparotomy for acute ruptured liver. The patient was not autotransfused and recovered. Associated low kidney function has long been recognized as a dangerous sequel to operations on patients with chronic liver disease. Coller, in his discussion of Orr and Helwig's paper, suggests that oliguria, under these circumstances, might be attributed to other physiologic alterations so often associated with poor liver function rather than to any specific toxin generated by the damaged liver.

The *spleen* is injured with considerable frequency. This condition may manifest itself by overwhelming shock, pain referred to the shoulder and extreme leukocytosis. On the other hand, many cases of delayed bleeding are reported.¹⁰⁻²²

An injured ballplayer, for instance, may even continue in the game for a while, or may not be suspected of a serious injury until exertion several days later produces a second burst of bleeding. McIndoe¹⁹ collected a total of 45 cases of bleeding delayed from two days to six months after the initial trauma. He classifies spleen injuries as follows: minor, superficial, capsular rupture or slight splenic contusion producing parenchymal ecchymosis; intrasplenic hematoma and subcapsular hemorrhage without capsular rupture; and capsular and parenchymal rupture with pericapsular hematoma. Rousselot²³ adds avulsion of the spleen from the hilus vessels. He calls attention to the over-all mortality of 30 per cent in injuries to the spleen, but in his group of 9 uncomplicated injuries, all the patients recovered. He made follow-up studies of these cases in order to determine that late secondary anemia does not occur following splenectomy. All authorities admit that splenectomy is the treatment of choice. Few advocate suture or tamponade. One known V-shaped rent in the spleen, discovered during laparotomy for a more severe injury, was left untreated and recovery took place.²⁴ Multiple complicating injuries and delayed improper treatment account for the high mortality.

Kidney injuries without penetration are of common occurrence. More of these of severe proportions have occurred since the high-speed automobile was developed. Authorities are somewhat divided regarding early surgery versus conservative measures. Nonoperative treatment certainly results in a successful outcome in the majority of kidney contusions. On the other hand, there are valid reasons for removing hematomas about the kidney.²⁵ All agree that one must determine the presence of a functioning kidney on the opposite side. Intravenous pyelography is the method of choice, although some authorities prefer retrograde pyelography, since this gives a better idea of the extent of the injury. Peacock²⁶ reports a fatal hemorrhage following retrograde pyelography for ruptured kidney. Robertson²⁷ and others stress conservative surgery when any is done. Turton²⁸ gives experimental data to support repair of the kidney. He also advises exploration through a loin incision except in cases with complicating intraperitoneal lesions. His dictum is, First, save the patient, then save the kidney. When the renal pedicle is torn, a rapidly developing mass in the flank will manifest itself; under these circumstances, nephrectomy is justifiable and usually necessary. Associated injuries to the descending colon require laparotomy. Cases demanding operation are naturally associated with a higher mortality than are those of less severe trauma.

The *pancreas* may be injured by blunt force, owing to its fixed position across the ridge of the spine. Few cases of successful immediate operation are reported. Cysts may form, which can later be removed or marsupialized.²⁹ Dixon³⁰ reports 2 cases of pancreatitis associated with rupture of the duodenum. There was no evidence of injury to the pancreas in either case. Both patients died and one was studied at autopsy. The condition cited implies a mystifying mechanism, since acute perforation of the duodenum from ulcer is rarely if ever associated with pancreatitis.

Hollow viscera, when ruptured, almost invariably result in death unless prompt action is taken to remedy the defect. The earlier operation can be undertaken, the better is the opportunity for a successful outcome. One must often explore the abdomen under these circumstances, to rule out a suspected perforation. There is little or no hazard from a negative exploration under modern conditions, and no apologies are needed for this procedure. It is not good judgment to delay exploration until the diagnosis can be confirmed by x-ray films that demonstrate free air in the peritoneal cavity, or to wait until the signs of peritonitis manifest themselves.

Whenever possible, rents in the stomach and intestine should be closed without resection. If the bowel has been stripped of its mesentery or the rent goes completely through the bowel into the mesentery, resection and anastomosis are justifiable. In colon wounds it is best to suture the opening if it is a small one and in a fixed portion of the bowel. If it is in the free mobile cecum or sigmoid, exteriorization is the method of choice. In perforations of the colon not exteriorized, a proximal vent should be established after suture. One must have in mind the possibility of traumatic thromboses of the large blood vessels, as such cases have been caused by blast injuries.² In the event of doubt concerning the viability of a segment of bowel, it is best to do a proximal complete colostomy.

It may be irrelevant to mention at this point injuries to the colon from compressed air. It seems, however, that this hazardous prank cannot be overemphasized. Brown and Dwinelle³¹ collected 60 such cases from the literature and added 3 of their own. It is interesting to note that as little as 4 pounds of pressure can cause rupture of the colon. The use of compressed-air hoses for dusting off workmen's clothing in industrial plants should be forbidden. The mortality in these injuries is 100 per cent without surgery and 42 per cent with it.

The *urinary bladder* may be ruptured by blunt force. Damage to this organ should be looked for in all traumas to the low abdomen. Injury

to the urethra and bladder are often associated with fractures of the pelvic bones. The simplest method of diagnosis is to catheterize the patient, if he cannot void. A large amount of bloody urine indicates a kidney lesion. Absence of urine or a few drops of bloody urine indicate bladder injury. Weyrauch and Peterfy³² have shown that cystometrograms are unreliable as a means of diagnosing a ruptured bladder. Peacock³³ reports 28 cases with only 4 deaths. Eighty-five per cent of his cases were associated with fracture of the pelvis. Early recognition and early operation were responsible for his good results.

PENETRATING WOUNDS

Penetrating wounds of the abdomen require less diagnostic acumen than nonpenetrating ones. If a large vessel is severed, death ensues so rapidly that the patient does not live to reach the surgeon. Thus, patients with lateral anteroposterior wounds are the ones he generally sees, whereas those with wounds in the midline seldom come to him before death. Gordon-Taylor^{3, 34, 35} points out that wounds penetrating the abdomen from one side to the other are more serious than those proceeding anteroposteriorly. Also, he calls attention to the combination of abdominal and chest wounds. Apparently, the left hypochondrium is more vulnerable than any other quadrant. Thoracic surgeons have developed the chest approach to this region—many of them prefer to attack the spleen and the upper end of the stomach by this route. Multiple injuries are as a rule more dangerous than single wounds; much depends, however, on the extent of the injury. The degree of hemorrhage is, according to Storck,³⁶ the most important factor in success or failure.

One should make a definite study of the course of the projectile. If there is only a wound of entry, a single film will locate the foreign body. It is not essential to remove it in all cases, but one should know in what region it lies. This gives the best clue concerning the organs most probably injured. Great stress is placed on buttock wounds, since they so often range upward. The fragment of shell casing or bullet may well lodge in the urethra or bladder, penetrate the rectum or traverse the abdomen. The most serious of all omissions is to overlook an injury to the colon, since recovery is extremely rare if perforation of this viscus is not recognized and properly treated.

In penetrating injuries of the abdomen, regardless of the direction of the projectile or its size, one must at the earliest possible moment determine by operation the extent of the injury and do the logical repair of the wounded parts. If there turns out to be only a superficial tract, traversing portions

of the abdominal wall, so much the better. Perforations of the stomach must be expected to have a wound of exit on the posterior wall. One should approach the deeper wound by dividing the gastrosolic omentum or by anterior gastrotomy. Wounds of the duodenum may involve both walls. Fraser²¹ cites a case of complete severance of the duodenum treated successfully by turning in both ends and doing a posterior gastrojejunostomy. Perforations of the small intestine should be sutured without resection wherever possible. The mortality is lower in wounds of the jejunum than in those of the ileum.³⁷ After operations on the small intestine for traumatic wounds, one should employ Wangenstein suction or, if possible, suction drainage by a Miller-Abbott tube or some modification of it.

The colon presents a more serious problem; many of the pertinent points regarding this structure have already been made in the section on nonpenetrating wounds. Ogilvie,³⁸ of the British Army, emphasizes the importance of exteriorization when possible and proximal colostomy if suture is accomplished. These are good general surgical principles and should be rigidly observed. Drainage to the site of injury is advocated, care being used to keep the end of the drain away from the suture line.

Chemotherapy is rapidly becoming standardized. The tendency to apply the sulfonamide drugs locally is now being seriously questioned. Kennedy³⁹ states that all combatants are furnished with some form of these drugs, to be taken by mouth, if possible, as soon as a wound is received. Doubtless it will be possible to give many of the injured sulfadiazine by the intravenous route at an early hour. This method was found of inestimable value in treating a large series of severe burns in a recent civilian catastrophe.⁴⁰ It seems probable that the local use of the drug will be reserved for emergency dressings or for its bacteriostatic effect in the treatment of contaminated wounds. The sulfadiazine level in the blister fluid of a burn is comparable to that in the blood stream.⁴¹ There is a widespread use of sulfanilamide powder intraperitoneally following any gastric or intestinal operation. There is a rapid absorption of this drug through the portal system. Lyons⁴² has pointed out that this may, under certain circumstances, be very dangerous to the liver. The greatest of all sins is to depend on this drug to offset faulty technic.

It appears that the secondarily invading or late developing staphylococcus, responsible for so many deaths and such prolonged sepsis and disability, may be curtailed or even eliminated by the use of penicillin.

Anesthesia in abdominal trauma is a controversial subject. Local anesthesia is advocated by very few. Spinal anesthesia is preferred by Storck⁴³ and Bove,⁴³ and Pentothal Sodium intravenously by Ross and Hulbert⁴⁴; the latter was also found useful by Moorhead⁴⁵ at Pearl Harbor. Strode⁴⁶ and many others conclude that ether is after all the safest and easiest anesthetic for most abdominal wounds.

Wound preparation has been dealt with by Reid and Carter,⁴⁷ Koch⁴⁸ and Kerrigan.⁴⁹ It is obvious that chemicals are of secondary consideration. Careful mechanical cleansing by neutral soap and water with cotton pledgets for ten minutes under sterile precautions obviates the use of antiseptics. The traumatic wound must be kept covered and the washing done away from, rather than toward, it. After this is done, the wound itself is irrigated with warm physiologic saline solution. Reid and Carter prefer to omit the wound irrigation. This is doubtless good advice to those who understand proper wound excision.

First-aid treatment of wounds of the abdomen should consist in the application of a sterile dressing only; this should be held in place by a suitable binder and not be removed until the patient is ready for the operating room. Too much stress cannot be laid on the possible contamination of wounds by ungloved and unmasked personnel prior to definitive treatment.

Ogilvie³⁸ has called attention to too wide an excision of skin. He says, "Skin is viable after trauma, resistant to infection and irreplaceable—no more must be removed than the bruised edge, that is, one-eighth inch at the most." He further points out that patients with abdominal wounds should not be transported early after operation, but should be allowed to recover from it before being moved any distance. Caution is given concerning the primary suture of traumatic wounds, since too many of them become septic. Delayed closure is advocated. It is important not to pack the wounds too tightly with vaseline gauze, and dressings must be made tight for transportation purposes. Plaster of Paris reinforcement during transportation has been found useful.

Tetanus antitoxin and gas-bacillus antiserum should be used following all civil wounds; the former can be omitted if it can be ascertained that the victim has previously been immunized with tetanus toxoid, but a "booster" injection of toxoid should be administered.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29041

PRESENTATION OF CASE

A seventy-one-year-old insurance broker entered the hospital because of inability to swallow solids or liquid food.

Three months prior to admission he gradually became unable to swallow solid food, choking whenever he attempted to ingest anything other than fluids. He then developed a similar trouble in swallowing liquids. Whenever he drank liquids he complained of pain and burning in the throat. The patient attributed his trouble to infected teeth, which were extracted on the day prior to admission. During his illness he lost approximately 40 pounds.

The family and past histories were noncontributory.

Physical examination revealed a markedly emaciated, weak, pale man who was having considerable difficulty because he seemed to be choking on mucus collected in the mouth and throat. At times he seemed slightly confused. The skin was thin, white and atrophic. The pupils were equal, round and reacted to light. There was a slight nystagmus on extreme deviation to the right or left, and a senile ectopion. The patient was edentulous, but there were several draining tooth sockets. The tongue was red, smooth and fissured. The pharynx was congested. Skin fissures were prominent at the angles of the mouth. The trachea was in the midline. Expansion of the chest was fair. There was impairment in resonance at the left apex anteriorly, and breath sounds were slightly suppressed at the right base posteriorly. No rales were audible. Cardiac dullness was percussed 8 cm. to the left of the midsternal line in the fifth intercostal space. The cardiac rhythm was totally irregular, but no pulse deficit was noted. A systolic murmur was audible at the apex. The abdomen was held tense, and there was a questionable generalized abdominal tenderness. There was pitting edema of the legs, feet and sacrum.

The blood pressure was 155 systolic, 60 diastolic. The temperature was 100°F., the pulse 68, and the respirations 20.

Examination of the blood revealed a hemoglobin of 8.9 gm. per cent, a red-cell count of 2,970,000

and a white-cell count of 11,200, with 47 per cent polymorphonuclear leukocytes, 7 per cent large lymphocytes, 29 per cent small lymphocytes, 14 per cent monocytes, 2 per cent unclassified cells and 1 per cent nucleated red cells. In the smear, there was a moderate variation in the size of the red cells; many were larger than normal, and rare microcytes were present. There was a moderate achromia, and the platelets were decreased slightly.

On the second day a barium meal was attempted. On fluoroscopic examination of the esophagus, the pharyngeal muscles appeared to be paralyzed. There was pooling of the barium in the hypopharynx, and the barium passed upward into the nasopharynx. The cervical esophagus was narrowed, and it was difficult to visualize this area because of the patient's weakness and the small amount of barium that passed through this area of narrowing. There was evidence of pressure on the esophagus by the thyroid gland at the level of the sternoclavicular joint, and the esophagus was displaced to the right. A small amount of barium spilled over into the bronchial tree.

When the patient returned from the X-ray Department he seemed to be choked up with barium. Suction was instituted, but he died approximately half an hour later.

DIFFERENTIAL DIAGNOSIS

DR. JACOB LERMAN: There is no statement about orthopnea or distention of the neck veins. The trachea was in the midline, and there were no palpable lymph nodes. The thyroid gland was not felt. Was the patient resting quietly lying down, or was he propped up in bed?

DR. TRACY B. MALLORY: There is no statement regarding orthopnea.

DR. LAURENCE L. ROBBINS: I did the fluoroscopy. The patient was not in particularly good condition, but so far as I could determine in the dark room he seemed like a good many patients who have considerable difficulty in breathing and swallowing at the time of examination. His condition did not seem particularly alarming; however, we did not give a great deal of barium. With the first mouthful of barium it was noted that there was widening of the hypopharynx and that the pyriform sinuses were completely filled. A small amount of barium spilled into the esophagus, but it seemed to be more from gravity than from muscular action; it was seen that the cervical esophagus was somewhat narrow. Whether there was actual intrinsic tumor there, I could not be positive, but on the spot films the mucosa looks pretty good. There is evidence of narrowing of the esophagus at the level of the sternoclavicular joint, and it is displaced considerably to the right side. On

this film you can see that the barium has spilled back into the nasopharynx, which is good evidence of paralysis of the pharyngeal and palate muscles.

DR. LERMAN: What about the trachea?

DR. ROBBINS: It is normal so far as I can see.

DR. LERMAN: Why did you say the thyroid gland was the cause of pressure?

DR. ROBBINS: Because of the location of the lesion. I cannot be sure, however, that it was not something else. On this film you can see flecks of barium that are in the right main bronchus, and some of them are even as low as the right-lower-lobe bronchus.

DR. LERMAN: We have a markedly emaciated old man who had considerable difficulty in swallowing, an obvious nutritional deficiency, a moderate anemia of the normochromic, slightly macrocytic type and x-ray evidence of pressure on the esophagus, with displacement toward the right. From the story I gather that the deficiency syndrome antedated the dysphagia. It is difficult for me to be certain of that. Could he have had deficiency of this degree after only three months of esophageal obstruction?

Let us consider the thyroid gland as the cause of his trouble. It is hard to believe that any thyroid tumor could compress the esophagus and displace it to this degree without involving the trachea. Certainly thyroid malignancy that could obstruct the esophagus almost completely would do so only terminally, at least according to my experience. Chronic thyroiditis can obstruct the esophagus by posterior extension of the process, but I do not see how it can displace the esophagus. Moreover, I have never seen chronic thyroiditis produce almost complete obstruction. A toxic nodular goiter that is substernal, such as this would have to have been, should be considered. It would at least explain the relatively rapid development of the deficiency syndrome. In cases of thyroid disease, if there is clinical evidence of one or another deficiency syndrome, one must suspect associated hyperthyroidism. I have seen several thyrotoxic patients with peripheral neuritis and other evidence of vitamin B deficiency. At the present time I have under my care a patient with hyperthyroidism and marked dysphagia, associated with glossitis and pharyngitis of the type seen in vitamin B deficiency, whose basal metabolic rate is $+55$ per cent. She has been on a poor diet because of anorexia more than anything else. I cannot imagine a thyroid nodule that could produce this much pressure on the esophagus without producing pressure on the trachea and other evidence of pressure in the superior mediastinum. Obviously there were no symptoms of hyperthyroidism. Therefore it seems to me that we have to discard toxic goiter

as a cause of the esophageal obstruction. On the other hand there should have been found at autopsy an ordinary nontoxic nodule, which was independent of the main cause of death.

Lymphoma has to be considered, but there is nothing specific in the record to lead to this diagnosis.

I shall now consider two diseases. Generalized deficiency, no matter how it develops, may produce the picture of Plummer-Vinson syndrome, which this patient may have had. However, it is usually associated with hypochromic anemia. I believe that Plummer-Vinson's disease is part of a vitamin B deficiency syndrome, and that this case represents one type. Many of these patients with deficiency are prone to develop malignancy of the mucosa—mouth, pharynx or esophagus. Consequently it is likely that there is malignancy in the upper part of the esophagus in this case. One can reason the other way around: he had esophageal malignancy to start with and the interference with swallowing of food caused development of the deficiency state. Against this course is the relatively short duration of the obstructive symptoms.

In addition, there is the cardiac picture, which was probably due to arteriosclerotic heart disease with auricular fibrillation and, possibly, congestive failure. Other than peripheral edema, there was no evidence of congestive failure. One might therefore suspect that the edema was due to deficiency disease (nutritional edema) and not to congestive failure. Thus I am left with the following diagnoses: carcinoma of the esophagus and nutritional deficiency, with an independent, nontoxic, nodular substernal goiter, and arteriosclerotic heart disease.

DR. FULLER ALBRIGHT: Is it unusual to have the esophagus displaced by carcinoma?

DR. LERMAN: It depends on where the tumor arises. Most malignancies of the thyroid are asymmetrical.

DR. ALBRIGHT: It would constrict it down but would not displace it?

DR. LERMAN: I cannot answer that.

DR. MALLORY: I can imagine displacement, Dr. Albright, especially if the tumor extended into the deep cervical nodes on one side of the neck more extensively than on the other.

DR. EDWARD B. BENEDICT: This is not the usual picture of carcinoma of the esophagus. To have paralysis of the muscles of the pharynx is not usual either; I have never seen that except in myasthenia gravis.

DR. ROBBINS: It is occasionally attributed to pseudobulbar paralysis. This looks a good deal like the hypopharynx in myasthenia gravis except

that one sees only weakness whereas this looks like nearly complete paralysis.

DR. BENEDICT: You said you thought the mucosa was normal.

DR. ROBBINS: So far as I could tell.

DR. BENEDICT: That would certainly be against carcinoma of the esophagus, if intrinsic, as well as against myasthenia.

DR. J. H. MEANS: How is myasthenia going to push the esophagus to one side?

DR. BENEDICT: That would not do it alone.

DR. ROBBINS: I do not believe that the location of the lesion had anything to do with the paralysis of the pharyngeal muscles, because the mass is too far away from the point where paralysis is most noticeable.

DR. MEANS: That paralysis bothered me no end. I do not see how you can hook it up with the same trouble from the diagnostic point of view.

DR. MALLORY: I might just as well confess that we are not going to explain the paralysis.

CLINICAL DIAGNOSIS

Carcinoma of esophagus.

DR. LERMAN'S DIAGNOSES

Carcinoma of esophagus.

Nutritional deficiency.

Nontoxic nodular goiter (substernal).

Arteriosclerotic heart disease.

ANATOMICAL DIAGNOSES

Substernal colloid goiter.

Benign ulcer of esophagus.

Arteriosclerosis, moderate: aortic, coronary and cerebral.

Pulmonary emphysema.

Emaciation.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This man had a very large substernal goiter, weighing 350 gm., which clearly was the cause of the displacement of the esophagus. He also had a benign ulcer of the esophagus at a much higher level; it was only 2.5 cm. below the epiglottis, too high to be in any way connected with the thyroid tumor itself. We have no explanation, as I said, for the pharyngeal paralysis. The possibility of peripheral neuritis did not occur to us and was not called to our attention at the time of autopsy. We did go through the cerebrum and medulla with some care, and there was no medullary lesion to account for the paralysis. I cannot eliminate the possibility of peripheral paralysis, although we have no evidence that other peripheral nerves were involved.

DR. LERMAN: The Plummer-Vinson syndrome has been described several times in association with paralysis of the pharynx. That is why I attributed the paralysis to the deficiency state.

DR. BENEDICT: What was the cause of death?

DR. MALLORY: There was extensive emphysema. There was mild coronary sclerosis without occlusion, and marked emaciation, which was noted clinically; we found nothing else.

DR. BENEDICT: He apparently did not inhale much barium.

DR. MALLORY: Traces of barium were found down to the end of the bronchial tree. On the other hand as much and more lipiodol is frequently instilled without any respiratory embarrassment. I am sure that the patient did not die of bronchial obstruction.

DR. ROBBINS: Many of the patients who have paralysis of the hypopharynx spill barium into the trachea in larger amounts than this man did without any sequelae.

CASE 29042

PRESENTATION OF CASE

A sixty-six-year-old plumber entered the hospital because of shortness of breath.

For many years he had had a chronic hacking cough that occasionally was productive of small amounts of sputum. Six months before entry, he had to give up working because of generalized weakness, and four months later he became short of breath after only moderate exertion. The dyspnea became progressively worse, and he became orthopneic. Four weeks before entry his cough increased and he raised several teaspoonfuls of sputum, which was pink stained at times. During the month prior to admission his arms, neck and jaws became swollen, particularly after lying down, and veins appeared over his chest. At no time did his ankles swell. His appetite was unchanged, and his weight had been maintained at 137 pounds.

The family history was noncontributory. Fourteen years before entry he was found to have a systolic blood pressure above 200. He never noted any frequency, urgency, hematuria, pyuria, nocturia, dysuria, costovertebral-angle tenderness or headache.

Physical examination revealed a well-developed man who was obviously dyspneic and orthopneic. There was a striking pitting edema of the upper extremities, and engorgement of the veins of the upper extremities and neck. There were many dilated veins over the chest to the level of the costal margins. There was slight cyanosis of the

lips. Many small matted lymph nodes were felt in the left supraclavicular fossa and left axilla. The trachea was deviated to the right. Over the right lung anteriorly and posteriorly there were greatly diminished breath sounds. There was no change in the transmission of fremitus or spoken voice. There was dullness at the right lung base posteriorly, and diaphragmatic excursions could not be demonstrated on that side. The cardiac dullness was percussed 7.5 cm. to the left of the midsternal line. The heart sounds were of good quality, and no murmurs were audible. The liver was percussed 5 cm. below the costal margin. The spleen was not felt. There was no edema of the lower extremities.

The blood pressure was 210 systolic, and 100 diastolic. The temperature was 98.8°F., the pulse 80, and the respirations 20.

Examination of the blood revealed a hemoglobin of 10.2 gm., a red-cell count of 3,200,000, and a white-cell count of 14,100, with 83 per cent polymorphonuclear leukocytes, 7 per cent large lymphocytes, 3 per cent small lymphocytes, 3 per cent monocytes, and 4 per cent myelocytes; there was a slight anisocytosis of the red cells. The urine was acid, had a specific gravity of 1.018, gave a ++ test for albumin, and contained numerous hyaline and finely granular casts. The Sulkowitch test for urinary calcium was ++. The blood non-protein nitrogen was 28 mg. per 100 cc.; the bicarbonate was 25.3 milliequiv., and the chloride 86.4 milliequiv. per liter.

A chest roentgenogram demonstrated a lobulated mass in the right upper mediastinum apparently arising from the tracheobronchial angle, with several smaller masses lateral to it. The heart was slightly displaced to the right and was slightly enlarged. The diaphragm was low on both sides, the right half showing impaired motion. The right lower lobe of the lung was decreased in size, as visible in the lateral view, and contained flecky areas of increased density. The soft tissues of the neck were enlarged, particularly on the right, and there were several areas of calcification on both sides. Venous-pressure studies were done with the patient sitting at a 60° angle with the bed. The pressure in the right antecubital vein, held at the level of the second costochondral junction, varied from 400 to 410 mm. of water (normal, 40-110 mm.) in three determinations, and showed a good pulse excursion. The simultaneous pressure in a vein over the internal malleolus was 100 mm. A biopsy specimen obtained from the left axilla showed only chronic inflammation. A bronchoscopy was suggested, but it was thought that the patient was too sick to withstand the procedure.

On the eighth day 150 r of x-ray therapy was given to the mediastinal mass. That afternoon he was found to be unresponsive. The entire body was flaccid. The pulse was 90, and the respirations 20. He was in an oxygen tent at that time. Two hours later he died. Terminally the respirations varied between 35 and 25.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN BRUES: May we see the x-ray films?

DR. LAURENCE L. ROBBINS: This is the lobulated mass that was described, with these other areas of density lateral to it; I note that the right lower lung field is less bright than the left. In the lateral view you can see that there are small areas of increased density posteriorly, so that the pulmonary lesion must be located in the lower lobe. The areas of calcification that were described in the neck are these. I think the diaphragm is low on the left, but that does not agree with the record, which states it was low on both sides.

DR. BRUES: It is helpful to have the right side high as well as paralyzed.

That is not a filling defect in the stomach, is it?

DR. ROBBINS: No; I do not believe so.

DR. BRUES: The differential diagnosis is that of upper mediastinal obstruction with compression of the vena cava, presumably including or below the azygos vein because of the venous distention and massive edema. Aside from that we have nothing but an enlarged liver and hypertensive renal disease, to which I shall refer only in the final diagnosis. Mediastinal compression can be due to tumor, benign or malignant,—infection or aneurysm. Taking up the possibilities, carcinoma of the lung, arising in the tracheobronchial angle, with metastases to the bronchial nodes would account for the greater part of the picture. I think the lesion and metastases were suitably located for this. We should have to include a lesion below, either a metastasis or a plugged bronchus, to account for atelectasis in that region—I take it that the lower lobe was atelectatic. Against the diagnosis of carcinoma of the lung we should consider the long history of cough. The history does not say for exactly how many years he had been coughing. It says "many years." I believe if that meant a year and a half or two years it would be consistent with cancer. Otherwise, we have to assume he was coughing for some other reason before the present illness. With calcification in the neck he probably at one time had tuberculosis of the cervical nodes, but we have no evidence of old pulmonary tuberculosis. The absence of weight loss is against carcinoma, but weight loss is certainly not always found in cancer. Hemoptysis is one of the early

symptoms indicating erosion of the bronchus and is therefore in favor of cancer.

This exact picture may also be produced by tuberculosis of the bronchial nodes; chronic tuberculosis of the mediastinum is common in children but extremely uncommon in adults, and therefore is very improbable. As for Hodgkin's disease, lymphosarcoma or leukemia, hemoptysis is not usually an accompaniment of these conditions. The localization of the mediastinal involvement to the upper mediastinum is somewhat more characteristic of carcinoma. Certainly, I should say that lymphoma or some other radiosensitive tumor is by no means out of the question. It is my second best diagnosis, and I think it was perfectly correct that radiotherapy in lymphoma doses was given; this should always be done in such a case if the diagnosis cannot be settled.

We must include in the differential diagnosis of mediastinal tumors, such conditions as benign tumors, teratomas and localized infections. These would be expected to displace things away from the lesion because they grow by expansion rather than by infiltration. We might consider aneurysm, but there is nothing to suggest it. There is no serologic report, but I should not go all out in favor of aneurysm even if the Hinton test were positive.

As for metastatic malignancy—it is anybody's guess where the malignancy might be. Perhaps an intra-abdominal tumor would be most likely to do this. If this is carcinoma of the lung, which I think on the basis of the whole picture is the best available diagnosis, there are metastases to the bronchial nodes. Most statistics show that the majority of carcinomas of the lung metastasize to the regional nodes and that the next commonest site is the liver. With an enlarged liver, we might therefore assume it to be involved. What about involvement of the adrenal glands? The chloride was low (86.4 milliequiv.), the blood having presumably been taken from the antecubital vein in the edematous area. There was obvious venous stasis. Under these circumstances one would expect the chloride to be low because of selective diffusion out of the bloodstream into the swollen interstitial space. I am not going to believe that the chemical findings indicate anything else, although bilateral adrenal metastases are frequently seen in cancer of the lung.

My diagnosis therefore is carcinoma of the lung arising in the right bronchus, with metastases to the bronchial nodes, and involving the vena cava and azygos vein by pressure or thrombosis and probably the phrenic nerve, since the paralyzed diaphragm is high and not low. I should say that there was partial atelectasis of the lower lobe due

to bronchial obstruction or compression from metastases, metastases to the liver but probably not to the adrenal glands; hypertensive heart disease, with slight vascular changes in the kidneys; and, finally, old tuberculous infection in the cervical nodes.

DR. J. H. MEANS: I saw this man just before he died. I was not confident that he had lymphoma, but thought he was entitled to treatment. However, there was evidence of such severe mediastinal pressure that we debated about giving it because of the question of acutely increasing the pressure and perhaps killing him. But finally, after consultation with the X-ray Department, it was decided to give a small dose. I talked it over with the Surgical Service and raised the question of whether splitting the sternum would offer a feasible method of relieving the upper mediastinal pressure, but they did not believe it advisable.

DR. JACOB LERMAN: When this patient first came in, without having seen the x-ray films but knowing that he had lymph nodes in the axilla and one very large one in the sternoclavicular region, I believed that he had lymphoma. After the x-ray examination the tendency was to swing away from this diagnosis toward carcinoma, either in the mediastinum or in the bronchus.

DR. RULON W. RAWSON: I saw this patient in the Out Patient Department. At that time he presented no lymph nodes, and we did not consider the diagnosis of lymphoma. The spleen was enlarged, and I was able to demonstrate that the liver was also enlarged.

CLINICAL DIAGNOSIS

Superior mediastinal tumor (? lymphoma or carcinoma).

DR. BRUES'S DIAGNOSES

Carcinoma of right upper bronchus, with metastases to bronchial nodes and liver.

Secondary compression or thrombosis of superior vena cava.

Atelectasis, right lower lobe.

Hypertensive heart disease, with slight renal vascular changes.

Old tuberculosis of cervical nodes.

ANATOMICAL DIAGNOSES

Bronchiogenic carcinoma, oat-cell type, with extension to mediastinum and lower cervical region.

Invasion of superior vena cava.

Obstruction of thoracic inlet.

Cardiac hypertrophy.

Nephrosclerosis.

Arteriosclerosis: coronary and aortic.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The autopsy showed a large tumor mass in the upper mediastinum, which encircled the trachea and great vessels. The mass was rather soft and on section was pink and shiny, suggesting sarcoma. However, a quite unusual finding was that the tumor had grown directly through the wall of the superior cava; tumor nodules were even present within the cava itself (actual invasion of the vessel wall by lymphoma is quite unusual). On opening the trachea a number of raised submucosal nodules were felt, and when the right bronchus wall was opened, a mucosal tumor appeared. On the basis that the mucosa of the bronchus was involved and the wall of the vena cava was eroded, we thought at the time of autopsy that cancer was more likely than lymphoma. When the histologic sections came through, the mass turned out to be an undifferentiated small-cell tumor, the cells of which were oval to slightly spindle shaped, so I am quite confident that it was an oat-cell carcinoma of the lung, not lymphoma. We found no distant metastases. There was a small nodule in the adrenal gland, but that turned out to be a cortical adenoma, so that the patient had an excessive rather than a diminished amount of cortical tissue. The liver and spleen were not involved. The deeper nodes of the neck did contain tumor similar to that in the mediastinum. There was also a mass of tumor tissue at the apex of the right lung, which formed sort of a pleural cap over the apex. He had severe emphysema, and I think that his many years of cough were based on that. There was some pulmonary fibrosis, also aspiration of blood into the right lower lobe, which I believe accounts for the density observed by the radiologist in that area.

The kidneys showed mild vascular changes, and

the heart was moderately hypertrophied, consistent with some years of hypertension.

DR. ROBBINS: Was the tumor of sufficient size to cause obstruction of the right main bronchus?

DR. MALLORY: A very small degree of obstruction only, I should think; there was nothing in the right lower bronchus to produce collapse specifically of the lower lobe as against the upper lobe.

DR. EDWARD B. BENEDICT: Is not bronchiogenic cancer an extremely rare cause of the upper-mediastinum syndrome?

DR. MALLORY: Yes, but we have seen it.

DR. BENEDICT: Is it not commoner in lymphoma?

DR. MALLORY: Yes, I think so, although of all mediastinal masses, bronchiogenic carcinoma is the likeliest to extend.

DR. MEANS: I should have thought carcinoma more likely to produce such a picture. It encircles the great vessels and squeezes them, whereas lymphoma presses on them.

DR. MALLORY: Lymphoma often invades the mediastinum diffusely. It rarely occludes the arteries, but it closes the veins by external pressure.

DR. RAWSON: But you would not expect lymphoma to invade the vessel wall?

DR. MALLORY: No; it certainly is uncommon.

DR. ROBBINS: What did you conclude regarding the immediate cause of death? I am interested because he had the radiation shortly before death.

DR. MALLORY: I think death was due to mediastinal compression, and I do not believe that the radiation made any difference—the patient would have died in approximately the same length of time regardless.

DR. ROBBINS: I wondered because of the amount of radiation he had. It was a fairly small amount and not sufficient to cause much swelling of the tumor, particularly in that length of time.

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NATIONAL SOCIAL HYGIENE DAY

NATIONAL Social Hygiene Day, to be observed this year on February 3, is dedicated to the program for the prevention and cure of venereal disease. Starting with the premise that gonorrhea and syphilis can be prevented and cured, we may well ask ourselves, What has been learned of this prophylaxis and therapy and how may we best utilize our present knowledge?

Adequate education of the layman and the physician must be assured by placing the proper teaching material in the hands of every person competent to use it. Syphilis and gonorrhea must be detected early and treated promptly and prostitution must be suppressed, for the greater the delay the more serious are the complications and the longer the time required for cure. So also must all contacts be sought out and treated and the transmission of

disease to future generations must be prevented by premarital examination. Findings from such investigations should be repeatedly confirmed during the early months of pregnancy. Finally, citizens, both physicians and laymen, must co operate in all phases of this effort.

No magic formulas or secret weapons have been developed, but great advances have been made and are still being made in the treatment of these diseases. The general program of this attack is outlined in the pamphlet "Social Hygiene Takes Battle Stations" issued by the American Social Hygiene Association.

Such a program should be active in every state of the Union. In this connection it is of considerable satisfaction to learn that it is being carried out in far distant Hawaii* where the venereal disease rate in the armed forces is lower than the average in the Army as a whole. This territory is one of the safest places in the Union from the standpoint of venereal disease among the army personnel. If Hawaii can accomplish this, all other parts of the country can and should do so, especially when we realize how normal living conditions have been disrupted there. The Health Department of Hawaii is to be congratulated on performing a task which Surgeon General Parran has outlined so well as follows: "The conquest of syphilis and gonorrhea is not a task for official health agencies alone, nor yet for physicians alone, but is still a task for the whole people. By the union of public and private efforts we can minimize syphilis and gonorrhea and the ill health, suffering and waste they cause."

*Allison S. D. Facing the facts about venereal disease. *Health* 39 1942.

EFFECT OF WARTIME FOOD ON CHILDREN IN GREAT BRITAIN

THE *Lancet*,¹ editorially, admits that there is as yet little information about child health during the war, and that many factors other than diet may be effective. Thus, it is known that war has resulted in an increased carbohydrate intake for all ages and classes, on account of the shortage of meat, fish,

eggs, milk and fruit, and in a leveling of the diet, since rationing and lack of mass unemployment have brought about a fairer distribution of food-stuffs. The diet of the majority has been impaired, and the diet of the poorest has been improved.

The figures that are available show a definite reduction in the average weight increase in 1940 and 1941 as compared with that in 1936-1939, a rise in infant mortality amounting to 6.5 per thousand live births, and an alarming increase in deaths from tuberculosis. Among children under ten years of age, the deaths from all forms of tuberculosis in 1941 exceeded those of 1939 by 45 per cent, and in children under five, the deaths from tuberculosis of the respiratory tract had nearly doubled. A survey,² published in the same issue of the *Lancet*, shows a definite drop, although to no serious degree, in the average hemoglobin level compared with that in prewar groups of school children, and a high incidence of anemia among infants under two years of age. It is admitted that the vitamin C intake is below the optimum, but there is no evidence that this deficiency has retarded the growth or affected the health of British children; doubt has also been cast on the adequacy of the official dosage of "cod-liver oil compound" recommended for infants under six months of age, although no figures exist concerning the incidence of rickets for the winter 1941-1942. Certainly, careful and continued studies are indicated.

On the whole, the diet is considered to be reasonably adequate, although necessarily far from perfect, and is improving; in sharp contrast is the lot of millions of children on the Continent, as observed by Dr. W. D. Robinson in Madrid and by Dr. Harold C. Stuart in unoccupied France and reported by Dr. Stuart³ to the Suffolk District Medical Society in October. There, with blood ascorbic acid levels invariably zero and low vitamin A levels, many early manifestations of deficiency syndromes were found, and the more recent reports indicate the appearance of even severer deficiencies.

A world on short rations requires very serious contemplation of its nutritional problems.

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MEDICAL EPONYM

GRAHAM STEELL MURMUR

This was described by Graham Steell (b. 1851) assistant physician to the Manchester Royal Infirmary, in the *Medical Chronicle* (Manchester) (9: 182-188, 1888) under the title, "The Murmur of High-Pressure in the Pulmonary Artery."

I wish to plead for the admission among the recognised auscultatory signs of disease of a murmur due to pulmonary regurgitation, occurring independently of disease or deformity of the valves, and as the result of long-continued excess of blood pressure in the pulmonary artery.

In cases of mitral obstruction there is occasionally heard over the pulmonary area (the sternal extremity of the third left costal cartilage), and below this region, for the distance of an inch or two along the left border of the sternum, and rarely over the lowest part of the bone itself, a soft blowing diastolic murmur immediately following, or, more exactly, running off from the accentuated second sound, while the usual indications of aortic regurgitation afforded by the pulse and so forth are absent. The maximum intensity of the murmur may be regarded as situated at the sternal end of the third and fourth intercostal spaces. When the second sound is reduplicated, the murmur proceeds from its latter part. That such a murmur as I have described does exist, there can, I think, be no doubt.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON LEGISLATION

Attention of the members of the Massachusetts Medical Society is invited to the following bills which are of interest to the medical profession and are at present before the Legislature.

HOUSE 437. AN ACT REPEALING THE PROVISIONS OF LAW REQUIRING PRE-MARITAL SEROLOGICAL TESTS.

Section 1. Section twenty B of chapter two hundred and seven of the General Laws, inserted by section one of chapter six hundred and one of the acts of nineteen hundred and forty-one and as most recently amended by section two of chapter six hundred and ninety-seven of the acts of nineteen hundred and forty-one, is hereby repealed.

Section 2. Section twenty-eight of said chapter two hundred and seven, as amended by section two of said chapter six hundred and one, is hereby further amended by striking out, in the third and fourth lines and in the thirteenth line the words "sixty days" and inserting in place thereof, in each instance, the words:—six months,—so as to read as follows:—

Section 28. On or after the fifth day from the filing of notice of intention of marriage, except as otherwise provided, but not in any event later than six months after

such filing, the clerk or registrar shall deliver to the parties a certificate signed by him, specifying the date when notice was filed with him and all facts relative to the marriage which are required by law to be ascertained and recorded, except those relative to the person by whom the marriage is to be solemnized. Such certificate shall be delivered to the minister or magistrate before whom the marriage is to be contracted, before he proceeds to solemnize the same. If such certificate is not sooner used, it shall be returned to the office issuing it within six months after the date when notice of intention of marriage was filed.

Section 3. Section fifty-seven of said chapter two hundred and seven, as amended by section three of said chapter six hundred and one, is hereby further amended by striking out, in the second and in the fifth and sixth lines, the words "sixty days" and inserting in place thereof, in each instance, the words:—six months,—so as to read as follows:—

Section 57. Whoever performs a ceremony of marriage upon a certificate more than six months after the filing of the notice of intention of marriage as set forth in such certificate and not having used it fails to return it within six months after such filing, to the office issuing the same, shall be punished by a fine of not more than ten dollars.

HOUSE 79. Bill providing for the inspection of colleges, universities and medical schools approved for the purposes of medical education and for withdrawal of such approval in certain cases.

This bill was referred to the Committee on Public Health.

HOUSE 80. Bill relative to examination for registration as qualified physicians.

This bill was referred to the Committee on Public Health.

HOUSE 81. Bill relative to the scope of examinations for registration as qualified physicians.

This bill was referred to the Committee on Public Health.

HOUSE 89. Bill relative to certain clinics conducted by the licensed hospitals.

This bill was referred to the Committee on Public Health.

HOUSE 98. Bill relative to payment of medical, hospital and other services to old-age assistance recipients.

This bill was referred to the Committee on Pensions.

HOUSE 252. Bill further regulating medical services rendered under the workmen's compensation law.

This bill was referred to the Committee on Labor and Industries; the hearing will be held on February 2.

HOUSE 352. Bill relative to payment of medical, hospital and other services to dependent children and their parents.

This bill was referred to the Committee on Public Welfare.

SENATE 11. Bill to provide for medical and hospital services and medicines for total and permanent disability cases under the workmen's compensation law.

This bill was referred to the Committee on Labor and Industries; the hearing will be held on February 2.

SENATE 62. Bill permitting the registration without examination of certain graduate nurses.

This bill was referred to the Committee on Public Health.

BRAINARD F. CONLEY, M.D., *Chairman*
Committee on Legislation

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

TRANSFUSION REACTIONS

During 1941, 4 deaths were attributable to reactions from incompatible transfusions.

The first case was associated with complete premature separation of the placenta at thirty-five weeks. The patient, who was twenty-nine years old, had had four previous pregnancies. The first went to term; a living child was obtained, and there were no complications. In the second, third and fourth pregnancies, the babies were born prematurely and were jaundiced, all of which suggests erythroblastosis foetalis. During this pregnancy there had been a little bleeding at the thirtieth week. The patient started labor prematurely and entered the hospital with intact membranes and slight bleeding, which continued with each contraction. When fully dilated, a macerated fetus and a completely separated placenta were delivered spontaneously; this was followed by massive hemorrhage and profound shock. An intravenous injection of glucose, to which the patient responded well, was followed by a 350-cc. transfusion of blood from her husband; the typing and cross-matching were done in the usual rapid fashion, but no incubation of the cross-matching was carried out. The transfusion seemed to have little or no effect. Three hours later, the patient's pulse again became very weak; she was given 500 cc. of blood from a registered donor, but the presence of Rh agglutinins and agglutinogens was not determined. The condition of the patient improved for three days; then she again became weak and was given 500 cc. of blood from her brother-in-law, which was again cross-matched in the usual rapid fashion but no test for Rh agglutinins and agglutinogens was done. Immediately following this transfusion the patient had a violent chill. The respiration became rapid, deep and labored; and from then on she went steadily downhill. A large trace of albumin appeared in the urine, and the sediment contained many casts; the nonprotein nitrogen was 300 mg. per 100 cc. Death occurred twenty-four hours later. An autopsy showed "hemolytic infiltration of the uterine wall, amyloid infiltration of both kidneys and spleen, and generalized edema." This death was apparently due to transfusions of blood,

none of which were tested for the presence of Rh factor; this is supported by the fact that the patient's previous three children had presumably suffered from erythroblastosis foetalis.

The second case was that of a woman who had had six previous pregnancies. The first three were normal. In the fourth, the baby died fifteen hours after birth. In the fifth, a cesarean section was performed because of placenta previa; and following the sixth, because of bleeding, a transfusion was given, presumably from a compatible donor. The patient was delivered vaginally, and the baby lived six hours. The baby showed typical signs of erythroblastosis. After the birth of the baby, the uterus was examined internally and a small rupture at the site of the previous cesarean section was found. A hysterectomy was immediately done. The patient was transfused, but an hour later she vomited blood, bled from the abdominal wound and went into profound shock. A total of 1600 cc. of blood was given, but the bleeding continued. The patient became anuric and jaundiced. Bilateral decapsulation of the kidneys was performed on the eleventh day. There was some improvement in the output of urine, but the patient continued to go downhill and died on the fifteenth day after delivery. It seems likely that this death was due to an Rh reaction.

The third case was that of a patient who had had one previous full-term normal delivery. In this pregnancy, the patient is said to have suffered a post-partum hemorrhage. Ten days after delivery, moderate bleeding again occurred, and a transfusion was given. Death occurred shortly thereafter and was probably due to an anaphylactic reaction, possibly involving the Rh factor.

The fourth case was that of a patient who had had a normal convalescence after a low-forceps delivery at term. Three and a half weeks after discharge from the hospital the patient was readmitted because of an abscess in the right breast. This was opened, and a culture showed *Streptococcus haemolyticus* and *Staphylococcus aureus*. A blood transfusion was followed by a severe reaction; a second transfusion was given twenty-four hours later. The patient developed anuria, with non-protein nitrogen of 80 mg. per 100 cc., and apparently died because she had been transfused with an incompatible blood.

These four cases evidence the seriousness of blood transfusion. It should never be done until it is certain that the blood is truly compatible. Two of these cases show that the Rh factor is the underlying cause of many anaphylactic deaths.

DEATH

HICKEY — JOHN J. HICKEY, M.D., of Peabody, died January 17. He was born in Marblehead and was in his

seventy-sixth year. He received his degree from the Harvard Medical School in 1903.

Dr. Hickey was a staff member of the Josiah B. Thomas Hospital and the North Shore-Babies Hospital. His memberships included the Massachusetts Medical Society and the American Medical Association.

His widow, three daughters and two brothers survive him.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATHS

CONANT — MARY C. CONANT, M.D., of Lyme, died August 26. She was in her seventy-first year.

Dr. Conant, the daughter of Jonathan J. and Martha (Howard) Conant, was born in Thetford, Vermont, and graduated from the Woman's Medical College of Pennsylvania in 1899. She carried on an institutional practice in Pennsylvania and New York for many years, and moved to Lyme in 1932. She was a member of the New Hampshire Medical Society and the American Medical Association.

She is survived by a brother and three nieces.

DAY — ARTHUR K. DAY, M.D., of Concord, died on December 31, 1942. He was in his eighty-first year.

A native of Dover, he moved to Concord in 1868 and had been a resident since.

He was a graduate of Harvard Medical School in 1889, and for twenty-five years served as attending physician at the Margaret Pillsbury General Hospital in Concord. During the Spanish-American War he served in the United States Army as a first lieutenant and assistant surgeon. Dr. Day was the school physician of Concord for a number of years.

Besides his widow, he is survived by a daughter, Miss Helen D. Day, and two sons, Captain Philip S. Day, U.S.A., and the Rev. Robert B. Day, of Niagara Falls, New York.

FROST — GILMAN D. FROST, M.D., of Hanover, died October 8. He was in his seventy-ninth year.

Dr. Frost, son of Dr. Carlton P. and Eliza (A. DuBois) Frost, was born in Randolph, Vermont, and graduated from Dartmouth Medical School in 1892. He had been a prominent member of the faculty of Dartmouth Medical School, having served as professor of anatomy from 1894 to 1910, as professor of clinical medicine from 1910 to 1937, as secretary and treasurer of the school from 1896 to 1904 and as treasurer from 1904 to 1909. For a number of years he was health officer of Hanover. He was a member of the New Hampshire Medical Society and the American Medical Association.

He is survived by his widow and four children.

HUTCHINSON — HERBERT S. HUTCHINSON, M.D., of Milford, died November 26. He was in his ninety-fourth year, and when he retired from active practice, a month before his death, he was the oldest practicing physician in New Hampshire.

Dr. Hutchinson, son of Stillman S. and Emeline G. (Lull) Hutchinson, was born in Milford in 1849 and graduated from Dartmouth College in 1875 and from Bellevue Medical College in 1880. He joined the New Hampshire Medical Society in 1882, and received the organization's fifty-year medal a decade ago. He was also a member of the American Medical Association.

He is survived by two sons.

MISCELLANY

TUBERCULOSIS AND THE WAR
—HERE AND ABROAD

Information from countries in the war area regarding present health conditions is limited and unsatisfactory. In certain European countries extreme hardship is being undergone, owing especially to nutritional inadequacies. Evidence is already appearing that the sharp rise in tuberculosis encountered during the last war may again be expected, and with increasing severity. Although the death rate from tuberculosis in the United States showed its usual decline last year, increasing effort must be made to maintain this favorable situation.

The United States

The world conflict of 1914-1918 for the first time revealed tuberculosis as a major problem. From the early discovery of large numbers of tuberculous troops in the French army to the final assemblage of mortality records of the war years in the civilian population of all countries engaged, it was evident that tuberculosis was exacting a great toll, unrecognized in the wars of previous years. There is every reason to believe, however, that long wars accompanied by privation have always led to an increase in tuberculosis. Crowding, malnutrition, exposure to infection and hardship of every sort have been considered responsible in different degree.

Fortunately, a quarter of a century of research since World War I has led to a better understanding of methods for the control of tuberculosis. Countries fearing the ultimate outbreak of hostilities, through the tense years preceding their final advent, anticipated tuberculosis as a grave menace and prepared accordingly. But in spite of forewarning and preparation, a rise in tuberculosis mortality rates appears already evident. Modern war is total war. Whole populations are engaged, through accelerated industry as well as actual combat.

In World War II, increasing effort is being made in the United States to avoid the induction of soldiers with tuberculosis. Measures ensuring a very examination of practically all recruits admitted to the armed forces are in effect.

In the civilian population, precautions are being taken against nutritional deficiency, since it is almost universally believed to have important bearing on the problem of resistance to tuberculosis. However, malnutrition may not be the gravest predisposing factor in a rise of tuberculosis. The acceleration of industry, leading to crowded quarters in industrial districts, brought about by mass migrations to industrial centers, has created another opportunity for widespread infection.

It is evident that a grave menace exists of another worldwide recrudescence of tuberculosis. Its prevention will require vigorous effort against the spread of infection and all measures possible to maintain a high level of resistance to disease. (Long E. R. *War and tuberculosis* *Am Rev Tuberc* 45 616-636, 1942)

Britain

To what extent the tubercle bacillus will repeat its former triumph of a generation ago in Britain cannot yet be properly gauged, but it has taken the initiative and the future course of events will be greatly determined by the effort put forward by tuberculosis workers.

Deaths from respiratory tuberculosis increased about 6 per cent the first year of the war, and 10 per cent the second, while the increase in deaths from other forms

of tuberculosis was 2.4 per cent the first year, and 17.6 per cent the second.

A considerable amount of infection is evidenced among the general population, particularly children, which means that either the infecting dose is large or the resistance low. Both causes may have operated in the first half of 1941 when the mighty bombing of towns and cities made contact infection probable and frequent. However, if the increase is found to have continued since more normal conditions have prevailed, it will strengthen the idea that there has been a general lowered resistance to infection in children under five. Many factors may have contributed to the lowering of resistance in children, among which are change in diet, nonpasteurized milk, blackout and shelter conditions, and lack of sleep and rest.

Comparing the trend of events during the first three years of the last war and the available figures for World War II, a definite similarity can be traced, although living conditions now are probably more conducive to the spread of tuberculosis. However, there are some marked differences. Tuberculous meningitis has increased sharply, whereas in the corresponding period of the last war it fell almost to the prewar level. A further point of difference is the small variation between the male and female curves.

These are ominous signs, which mean that infection is lurking in hidden places and taking its toll, especially in infant lives, and which emphasize the urgency of means for discovering these nests of infection and the need for their adequate control. (Heaf, F., and Rusby, L. *A further review of tuberculosis in wartime* *Tubercle* 23 107-130 1942)

France

Food rationing started throughout France on October 1, 1940, when the following foods were restricted: bread, meat, cheese, fats, sugar, milk, chocolate and milled products. Technically other foods could be obtained, but in reality it was difficult to get them. The results of a survey carried on by the Institut des Recherches d'Hygiène on how different families of Paris were feeding themselves showed a total caloric insufficiency of about a thousand calories daily, a calcium deficiency and a calcium phosphorus imbalance, and an insufficient intake of Vitamin A.

Undoubtedly morbidity and mortality from tuberculosis have noticeably increased in Paris. The percentage of rapidly developed tuberculosis has gone up in an alarming manner. Comparing the figures of the first six months of 1941 with the corresponding ones in 1939, the mortality from tuberculosis increased 10 per cent.

Four basic diets were prescribed for sick persons in four specific categories. To lessen the ill effects on persons with active tuberculosis and known lesions, a diet was given that corresponded to their general category, plus a supplementary amount consisting of 45 gm of meat and 15 gm of fat daily per patient. Despite the precaution indicated the march of tuberculosis up to October, 1941, had been ominously progressive, thus if the present dietary regime continues and the consequences increase, the problem of tuberculosis in France will be exceedingly grave. (Minoli, R. F. *Food rationing and mortality in Paris 1940-41* *Mill and Mem Fund Quart* 20 213-220, 1942)

Canada

The fall in the death rate from tuberculosis in Canada, which has been so evident for the past quarter of a

century, has occasioned in some quarters a false sense of security. Nothing could be more unsound or misleading. A disease that kills nearly 6000 of the population, leaves at least 30,000 incapacitated, and costs the country directly at least \$8,000,000 annually is still a formidable enemy and a major public-health problem.

If control of tuberculosis is to be maintained in wartime, tuberculosis services must be continued, problems that arise as a result of the war must be attacked and advantage taken of wartime case-finding projects. Case finding has kept ahead of treatment facilities, which have been inadequate, and until both are developed to a greater degree, control of tuberculosis is still hidden in the future.

Two of the most important phases of case-finding services available are for the general practitioners to provide an early diagnosis, since this is still the greatest source of cases, and examination of contacts, the next greatest source.

Two opportunities have presented themselves as a result of the war: the x-ray examination of all recruits for the armed forces and case-finding projects among industrial workers, particularly in war industries. Tuberculosis is two and a half times as great in industry as in the general population. Therefore, the control of tuberculosis is an important phase of industrial hygiene.

Emphasis is being placed on retaining the open case of tuberculosis in sanatoriums. Every patient who leaves against advice represents a weakness in the tuberculosis-control system. The factors involved should be carefully analyzed and every way possible must be sought to remedy conditions in institutions to offset this failure in efficient segregation. (Wherrett, G. J. *The control of tuberculosis in wartime*. *Canad. Pub. Health J.* 33:438-445, 1942.) — Reprinted from *Tuberculosis Abstracts* (January, 1943).

CORRESPONDENCE

SUSPENSION OF LICENSE

To the Editor: This is to inform you that on January 20, 1943, the Board of Registration in Medicine voted to suspend for one month the license to practice medicine in this Commonwealth of Dr. Louis R. Medverd, 1210 Cambridge Street, Cambridge, Massachusetts.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Source Book of Medical History. Compiled, with notes, by Logan Clendening, M.D. 8°, cloth, 685 pp. New York: Paul B. Hoeber, Incorporated, 1942. \$10.00.

There have been forthcoming in recent years several medical source-books, but none, however, with quite the range of this one. It aims at the whole of medicine, starting with the Egyptian papyri and ending with Roentgen, so that there is something in it for every man who finds pleasure and profit in reading,—if not *ipsissimis verbis*, the next thing to it,—a first-hand translation of what many important contributors to medical science had to say.

True, neither this nor any other book of the sort can attain perfection in every eye. There will be complaints no doubt that this has been left out which ought to have been included, and that that has been inserted which has

left too little space for something else. And, as is always the case, there are authors who suffer from the brevity of their allotted room—men, if you will, who lend themselves ill to cutting. Pasteur is one such.

But it would be ungrateful to complain too much; and in all this is a noteworthy and valuable assemblage of material, a great deal of which is inaccessible elsewhere. To list the distinguished contributors would be a pleasure, but space does not permit. For each, the editor has furnished a brief note to assist in placing man and matter in historical position, and for those who would go farther in any particular direction he has listed references.

This volume also deserves commendation as a piece of bookmaking. But, if a personal note may be hazarded the price, even in an era of increasing costs, seems a little high. There are no plates to add to the publishing expense, and it is a pity that the cost will be a deterrent to many who would like to see it on their shelves.

Medical Diseases of War. By Sir Arthur Hurst, D.M. (Oxon.), F.R.C.P. With the co-operation of H. W. Barber, M.B. (Cantab.), F.R.C.P.; H. B. F. Dixon, M.D. (Dub.), F.R.C.P.; F. A. Knott, M.D. (Lond.), M.R.C.P. T. A. Ross, M.D. (Edin.), F.R.C.P.; and Arnold W. Stott M.A. (Cantab.), F.R.C.P. Second edition. 8°, cloth, 42 pp., with 8 plates. Baltimore: The Williams and Wilkins Company, 1941. \$5.50.

This book, a new edition of one first published in 1916 and later republished in 1918, will be found especially helpful to neurologists and to all interested in the neuroses of war. It is largely based on the author's wide experiences in World War I as neurologist to Guy's Hospital, commanding officer of the Seale-Hayne Hospital for Functional Nervous Disorders and consulting physician to the Salonica Army.

When one realizes that almost 6 per cent of 341,025 discharges from the British Army (from 1914 to the end of April, 1918) were due to war neuroses, the importance of recognizing and treating these cases correctly is evident. Hurst's remarks in Chapter I, "Predisposing Causes of War Neuroses," will repay careful reading. Other chapters follow: "Hysterical Symptoms in Soldiers," "Hysterical Contractures," "Hysterical Postures and Gaits," "Hysterical Tremors" and "Hysterical Blindness," with numerous brief case records, which are instructive. Many results and cures were almost miraculous.

Of especial interest is Chapter XVI, "Anxiety Neurosis of War," by T. A. Ross. Here, in particular, psychotherapy, with explanation to the patient, persuasion and re-education, worked wonders. The chapter on "soldier's heart" is excellent; in great measure, it is based on Sir Thomas Lewis's book, published in 1918. The section by H. W. Barber, on skin disease, is of particular value and importance.

Although this volume is supposed to discuss the medical diseases of war, almost half is given over to the neuroses and almost another half to a number of medical diseases such as trench fever, typhoid and paratyphoid fevers, bacillary dysentery, epidemic jaundice and tetanus, that will probably be of little importance in World War II, because conditions are so different from those in 1914-1918. Epidemics and perhaps pestilence will probably occur, but they are to be expected among the civilian populations.

Of great value at the end of each chapter are references to the published literature. An index also adds to the general usefulness of the volume. It can be recommended to those who are interested in military medicine.

(Notices on page x)

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PYOGENIC LIVER ABSCESSSES DUE TO *KLEBSIELLA PNEUMONIAE* (FRIEDLAENDER'S BACILLUS)*

THOMAS D. KINNEY, M.D.,† and HAROLD S. GINSBERG, M.D.‡

BOSTON

FRIEDLAENDER'S BACILLUS has not often been recognized as an etiologic agent in liver abscesses. In 1892, Potter¹ reported the finding, at autopsy of a sixteen year old girl, of a liver abscess from which *Klebsiella pneumoniae* was recovered. Other cases have been reported by Chaher,² Courmont, Dujol and Devic,³ Elrison,⁴ Carnot, Dumont and Libert,⁵ Le Sourd and Drulard,⁶ Hegler and Nathan,⁷ Bachr, Schwartzman and Greenspan,⁸ Boettger, Weinstein and Werne⁹ and Rothenberg and Linder.¹⁰ In none of the cases was there any mention of the serologic type of the organisms recovered. It is the purpose of this paper to report 7 cases with autopsy findings in which serologic studies were carried out in an effort to identify the type of *K. pneumoniae*.

MATERIAL

The material presented is selected from 5699 autopsies performed during the years 1934 to 1941 inclusive at the Mallory Institute of Pathology of the Boston City Hospital. During this time, 52 cases with liver abscesses of all types were found, a general incidence of 0.9 per cent. It is of some interest to compare these figures with those reported by Keefer¹¹ from this institute in 1934-75 cases of liver abscesses in 10,309 autopsies, an incidence of 0.7 per cent, for the years 1896 to 1933 inclusive. Bacteriologic studies were carried out in 32 of the cases reported by Keefer. In no case was *K. pneumoniae* identified as the etiologic agent. In the present series, bacteriologic studies were carried out in 30 cases, and *K. pneumoniae* was identified in 7, or 23 per cent.

CASE REPORTS

CASE 1 C.B.T. (BCH 791,965), a 64 year-old man, was admitted on July 11, 1935, complaining of intermittent fever, chills and cough.

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Two months prior to admission, the patient noticed that his breath had a foul odor. He stated that he had lost 14 pounds. Two weeks before entry, he began to suffer from "nervous indigestion." This was followed a week later by the sudden appearance of attacks of severe chills, fever and sweating. These episodes lasted from 10 to 12 hours, after which he felt well until the next similar attack. Two days before admission, he developed a dry hacking cough. He also noticed thirst and polyuria. There was a history of diabetes of 3 years' duration.

On admission the temperature was 101°F, the pulse 98, the respirations 24, and the blood pressure 120/80. The patient was well nourished and normally developed. The skin was warm and dry. The breath had a disagreeable and nauseating odor. The teeth were absent. The tongue was dry and coated. The prostate was large and boggy. There was a left indirect inguinal hernia. The remainder of the physical examination revealed nothing of note.

The hemoglobin was 76 per cent (Sjoh), and the white-cell count was 13,600. A differential count showed 58 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 9 per cent monocytes and 1 per cent eosinophils. A strain of *K. pneumoniae* that did not ferment lactose was cultured from the urine. The urine showed various quantities of sugar but was otherwise normal. The blood Kahn and Hinton reactions were positive. Agglutination tests for typhoid, typhus and undulant fever were negative. Fasting blood sugar determinations varied between 185 and 420 mg per 100 cc.

The patient remained on the ward for 13 days, during which he experienced a severe chill on alternate days. On two occasions a strain of *K. pneumoniae* that did not ferment lactose was cultured from the blood. Treatment was supportive. On the 13th day, the patient suddenly complained of marked shortness of breath. He became orthopneic and semicomatose, and died ½ hour after onset of these acute symptoms.

Autopsy (A 35 417) Nothing of note was found on external examination of the body. The liver, whose edge extended 8 cm below the xiphoid in the midline and 3 cm below the costal margin in the midclavicular line, weighed 2600 gm. The entire dome of the right lobe was fluctuant, and the capsular surface over this area was a mottled white and deep reddish blue. The capsular surface elsewhere was firm and a homogeneous reddish brown. On section of the right lobe, an abscess 12 cm in diameter was found. The cavity of the abscess con-

tained 150 cc. of thick, brownish-yellow glairy mucopurulent material, together with what appeared to be lumps of necrotic liver tissue. Sections taken from the wall of the liver abscess showed marked necrosis, with polymorphonuclear leukocytic and macrophagic infiltration. In sections taken from areas of the liver not adjacent to the abscess, large numbers of polymorphonuclear leukocytes were found in the sinusoids, together with small masses of bacilli, which were both intracellular and extracellular. There was a partially organized thrombus in one of the radicles of the hepatic arteries. Patchy groups of liver cells were vacuolated. The gall bladder and bile ducts were negative.

The spleen weighed 180 gm. The remainder of the gastrointestinal tract was not remarkable. There were also moderate atheromatous changes in the coronary arteries, an acute tracheobronchitis and aortic atherosclerosis.

K. pneumoniae and *Clostridium welchii* were grown from cultures of the liver abscess, pericardium, heart's blood, pleura and right upper lobe of the lung. The former did not ferment lactose.

CASE 2. G.K. (B.C.H. 952,616), a 45-year-old man, first entered the hospital on July 2, 1938, complaining of a weight loss of 30 pounds in 5 weeks. In March, he had had an attack of diarrhea during which he had from ten to twelve stools daily. In May, he began to suffer from sharp pain localized in the right lower chest along the anterior costal margin; this was definitely worse on coughing and respiration. In June, he began to suffer from anorexia and fatigue. The family and past histories were irrelevant, except for excessive use of alcohol.

Physical examination showed only slight right-upper-quadrant tenderness. The red-cell count was 4,400,000 with a hemoglobin of 85 per cent (Sahli), and the white-cell count was 12,600, with 75 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes and 6 per cent monocytes. The blood Hinton reaction was negative. Nothing of note was found in the urine. On repeated tests of the stools 0 to +++ guaiac reactions were obtained; no parasites were found. Stool cultures were negative for pathogenic organisms. A blood culture showed no growth. Agglutination tests for the enteric group and *Brucella melitensis* were negative. A chest plate showed the right diaphragm to be slightly elevated.

The patient remained in the hospital 21 days. For the first 2 weeks he had a temperature that daily spiked to 101°F. but was afebrile during the 3rd week. Because he felt well, the patient left the hospital against advice.

The patient re-entered the hospital a month later, complaining of a recurrence of his original symptoms. He stated that his pain, which had shifted to the epigastric region, was gnawing, and that it was necessary for him to walk bent forward because of the pain. The temperature was 100.4°F., the pulse 104, the respirations 20, and the blood pressure 140/90. Physical examination was essentially the same as that at the time of his first admission.

The red-cell count was 3,310,000 with a hemoglobin of 61 per cent (Sahli), and the white-cell count was 18,800 with 78 per cent polymorphonuclear leukocytes, 4 per cent large lymphocytes, 17 per cent small lymphocytes and 2 per cent eosinophils. The white-cell count remained elevated during the remainder of the hospital stay. The alkaline blood phosphatase was 16.5 Bodansky units per 100 cc. The van den Bergh reaction was less than 1 mg.

per 100 cc. The nonprotein nitrogen was 25 mg., the phosphorus 2.7 mg. and the calcium 9.2 mg. per 100 cc. Nine stools gave + to ++++ reactions to benzidine. No parasites were found in the stools. The bleeding time was 4½ minutes, and the clotting time 5 minutes. A sputum culture yielded a Type 13 pneumococcus and an alpha-hemolytic streptococcus. A blood culture was positive for *K. pneumoniae*, which was not acted on by Type A serum.

An x-ray film of the chest showed an area of cloudiness at the tip of the right diaphragm. The gastrointestinal series was interpreted as showing a duodenal ulcer with periduodenal adhesions.

The patient had a high, spiking temperature during his hospital stay and continued to complain of abdominal pain and to suffer from profuse sweats. In spite of supportive treatment, he died on the 31st hospital day.

Autopsy. (M.L. 30830.) The body was that of an emaciated man. The peritoneal surfaces were smooth and glistening. The liver weighed 2840 gm. and was adherent over the right lobe to the diaphragm. Attempts to separate these adhesions resulted in the opening of abscess cavities, which were filled with glairy, yellow, purulent matter. The abscesses in the liver were multiple, and varied in diameter from 0.5 to 6 cm. These were abundant throughout the left lobe and the upper portion of the right lobe, the external portion being fluctuant over considerable areas. Some of the abscesses, on the other hand, were relatively firm. Most of them were made up of single large cavities, but others showed a central cavity with yellow, opaque extensions about the border into the neighboring liver tissue.

Histologic sections showed massive destruction of liver tissue, with complete obliteration of the hepatic architecture. Around the periphery of the abscesses were large numbers of polymorphonuclear leukocytes and lymphocytes that infiltrated the remnants of the intact liver tissue. Bacilli, both intracellular and extracellular, were present in the abscesses.

The stomach was adherent over the internal surface of the left lower and spigelian lobes and lobus quadratus. It was impossible to separate the stomach wall from the liver. The mucosa of the stomach, even that portion above the esophageal junction, was greenish black. Patches of green necrotic material occupied the summits of the rugae of the upper fundus, where the wall was adherent to the posterior surface of the liver. In the lower fundus, the surface was irregular and firm, without evidence of stomach wall, and section disclosed necrotic underlying liver tissue, with no evidence of stomach wall. The duodenum was normal. Sections from the portion of the stomach adherent to the liver showed the wall to be completely necrotic, whereas those from uninvolved areas of the stomach revealed no lesion. The spleen weighed 400 gm. and was somewhat soft in consistence, but was not remarkable otherwise.

In addition, there were moderate atherosclerosis of the coronary arteries, bronchopneumonia of the left lower lobe and atelectasis of both lower lobes.

K. pneumoniae was grown from the heart's blood and from the liver abscesses. The capsule of this organism was not affected by Type A serum.

CASE 3. C.F. (B.C.H. 931,709), a 71-year-old man, entered the hospital on February 27, 1939, too acutely ill to give an adequate history. The temperature was 101.4°F., the pulse was imperceptible, the respirations were 48, and the blood pressure was 80/60. The patient was in acute distress and markedly orthopneic, and the lips were

cyanotic. The skin was moist, cold and pale. The heart was enlarged to the left, and the sounds were muffled. Respirations were rapid and noisy, and there were fine, moist rales at the bases of both lungs. The abdomen was moderately distended, and the liver was enlarged to 5 fingerbreadths below the right costal margin. There was marked pitting edema of both legs. No laboratory work was performed.

The patient was given symptomatic and supportive treatment. He was digitalized rapidly. His condition became progressively worse, and he died the day after admission.

Autopsy (A 39 191) External examination of the body was negative. The liver weighed 1800 gm., was slightly increased in size and weight, was of a flabby consistence and was studded throughout by multiple, irregularly shaped abscess cavities containing very thick, mucoid yellowish brown exudate. The abscesses varied in diameter from 1 to 5 mm., and their walls were thin and shaggy. The wall of the gall bladder was markedly thickened, and the lumen contained three calculi varying from 10 to 14 cm in diameter. The common duct could not be identified. Histologic sections of the liver showed marked post mortem changes. There was a slight increase in the perportal connective tissue, together with moderate lymphocytic infiltration of these areas. There were multiple small abscesses in which the liver parenchyma was destroyed and replaced by polymorphonuclear leukocytes, bacilli and debris. The wall of the gall bladder was thickened by fibrous tissue and infiltrated by lymphocytes.

The spleen was markedly enlarged, weighing 1000 gm. and grossly showed no abnormalities. The splenic vein was normal. Microscopically, the pulp was diffusely infiltrated by polymorphonuclear leukocytes and markedly engorged by red blood cells.

The heart was moderately enlarged. There were pulmonary congestion and edema, and moderate benign prostatic hypertrophy.

Cultures from the hepatic abscesses revealed *K. pneumoniae* and an alpha hemolytic streptococcus. Splenic culture revealed *K. pneumoniae*. The heart's blood was not cultured. The capsule of the Friedlander's bacillus did not react with Type A serum.

CASE 4 W P (BCH 955,438), a 65 year old man entered the hospital on September 21, 1939. He was drowsy and orthopneic, and was unable to give any history. From the patient's physician, it was learned that, 1 month before entry, the patient had complained of malaise. Examination of the urine at that time gave a positive test for sugar, which cleared following a restricted diet. Approximately 10 days before entry, the patient developed painless jaundice. On examination, the liver edge was palpated 2 fingerbreadths below the costal margin, and there was right upper quadrant tenderness. Two days before admission, the jaundice became severer, and the patient became semistuporous.

At the time of admission, the blood pressure was 100/50, the pulse 110, the respirations 35, and the temperature 101.8°F. The patient was obese, stuporous, dyspneic and breathing with Cheyne-Stokes rhythm. He appeared to be in extremis. The skin and mucous membranes were markedly icteric. Moist rales were present over the entire lower two thirds of each lung. The liver edge was palpated 1 handbreadth beneath the costal margin and was tender on pressure. The remainder of the examination revealed nothing of note.

The red-cell count was 3,500,000 with a hemoglobin of 65 per cent (Sahli), and the white-cell count was 18,300

with 87 per cent polymorphonuclear leukocytes, 7 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils. The blood smear showed many young forms of the granulocytic series. The icteric index was 180. Tests for bile and urobilinogen were positive in 1:64 dilutions of the urine, which was otherwise normal. The blood Hinton reaction was normal. Lumbar puncture revealed nothing of note.

The patient was given supportive treatment but failed to respond and died a few hours after admission.

Autopsy (A 39 633) The body was that of a moderately well nourished and well developed man. There was marked icterus of the skin and sclerae. Examination of the peritoneal cavity was negative. The liver weighed 2400 gm. Several irregular mottled yellow areas beneath the intact capsule contrasted with the reddish brown parenchyma. On section, multiple abscesses, measuring a few millimeters to 8 cm in diameter, were present. Microscopic sections of the liver showed marked replacement of the liver cells by scar tissue. There was polymorphonuclear leukocytic and lymphocytic infiltration about the smaller bile ducts, with moderate polymorphonuclear leukocytic infiltration of the ducts. Sections taken from the edges of the abscesses showed massive tissue destruction, together with masses of polymorphonuclear leukocytes. Groups of bacilli were present in the abscesses and were both intracellular and extracellular.

The mucosa of the common duct was dull red, and sections showed slight polymorphonuclear leukocytic infiltration. There was no evidence of stone or obstruction in any of the large bile ducts. The gall bladder was enlarged but was thin walled, and microscopic sections showed a slight degree of chronic cholecystitis.

The spleen weighed 300 gm., but was otherwise normal. The pancreas was grossly normal, but microscopic sections showed focal areas in which the intralobular and extralobular fat was necrotic and infiltrated by polymorphonuclear leukocytes. There was also moderate focal infiltration by polymorphonuclear leukocytes between the acini.

Bronchopneumonia and benign nephrosclerosis were present.

Cultures from the heart's blood showed *Escherichia coli*, from the bile, *K. pneumoniae*, *Cl. welchii* and *Esch. coli*, from the liver abscesses, *K. pneumoniae* and *Cl. welchii*, and from the right and left lower lobes *K. pneumoniae*, pneumococcus (Type 29) and *Cl. welchii*. In each instance the *K. pneumoniae* showed no reaction with Type A serum.

CASE 5 E G (BCH 958,180), a 41 year old woman entered the hospital with a chief complaint of right upper quadrant pain radiating to the right subscapular region, and progressively increasing jaundice for the previous 3 days. The patient had been nauseated and had several bouts of vomiting before admission. No bile was seen in the vomitus. She had had no chills or sweating, but had had a fever. There had been no constipation or diarrhea. The stools were clay colored.

The patient had had many previous admissions to the hospital, several for rheumatic heart disease with mitral stenosis, auricular fibrillation and symptoms of decompensation, for which she was given digitalis. For the preceding 15 years, she had had symptoms relating to the biliary tract, for which she first had biliary drainage with removal of gallstones and later cholecystectomy and removal of calculi from the common duct. She had continued biliary symptoms with operations for removal of common-duct stones, and finally anastomosis of the com-

mon bile duct to the duodenum was performed 7 months before admission, because of a stricture of the common duct.

The blood pressure was 120/80, the temperature 103°F., the pulse 100 to 120, and the respirations 30. The patient was markedly jaundiced, thin and dehydrated. The diaphragm was not elevated, and a few basal rales bilaterally were heard in the lungs. The heart was moderately enlarged to the left and right, and the rate was rapid and grossly irregular. No murmurs were heard, and there were no thrills. There was no rigidity of the abdomen. There was tenderness in the right upper quadrant and epigastrium, but no masses were felt. The liver and spleen were not palpable. Peristaltic movements were present. Otherwise, physical examination was negative.

The urine showed a slight trace of albumin, rare white cells, and a +++ test for bile, but was otherwise normal. The red-cell count was 3,580,000 to 3,260,000 with a hemoglobin of 70 per cent (Sahli), the white-cell count 18,000 to 29,800, and the icteric index 95. The fasting blood sugar was 96 mg. and the nonprotein nitrogen 47 mg. per 100 cc. The stools were clay colored. The blood Hinton reaction was negative.

The patient was placed on bed rest, with a high-carbohydrate intake. She was given one injection of vitamin K intramuscularly. She seemed to be improving but the jaundice did not decrease. On the 3rd hospital day she became very orthopneic and disoriented, and died on the following day.

Autopsy. (A-40-541.) The body was that of a well-nourished, markedly jaundiced woman. The peritoneal cavity contained no free fluid, and the surfaces were smooth and glistening. The liver weighed 2120 gm. and on section showed multiple abscesses scattered throughout, measuring from 0.4 to 1.5 cm. and filled with thick mucoid yellowish-green pus. Microscopically, sections showed marked necrosis of the parenchyma, with massive polymorphonuclear leukocytic infiltration and abscess formation. Many bacilli were present. The bile radicles were moderately dilated. The common duct was greatly dilated, measuring 3.0 cm. in circumference, and thickened, and had a functioning anastomosis to the duodenum. The gall bladder and cystic duct were absent. No calculi were found in the common duct. The spleen weighed 310 gm. and was normal.

There were healed rheumatic heart disease, with mitral stenosis, pulmonary congestion and edema, purulent leptomeningitis, and slight, healed pyelonephritis.

Cultures of the liver abscess showed *K. pneumoniae*. The capsule of this organism was not reacted on by either Type A or Type B serum. Cultures of the meninges yielded a Type 14 pneumococcus.

CASE 6. P. S. (B.C.H. 1,005,913), a 56-year-old man, entered the hospital on May 4, 1941, complaining of a "cold" of 3 weeks' duration. He had been previously treated for diabetes mellitus in this hospital in November, 1940, and discharged on diet and insulin. He apparently did well until 3 weeks before entry, when he developed an upper respiratory infection. Two days before admission, he began to suffer from severe, persistent left-upper-quadrant pain, together with loss of appetite and dizziness.

The temperature was 99.2°F., the pulse 90, and the respirations 22. The blood pressure was 110/80. Physical examination showed a man who presented evidence of weight loss. There were moist rales at the base of the left lung. There was a systolic murmur at the base of

the heart. A left indirect inguinal hernia was found. The remainder of the physical examination was negative.

The red-cell count was 4,400,000 with a hemoglobin of 88 per cent, and the white-cell count was 15,800 with 75 per cent polymorphonuclear leukocytes, 15 per cent small lymphocytes, 2 per cent large lymphocytes, 7 per cent monocytes and 1 per cent basophils. The blood non-protein nitrogen was 25 mg., the calcium 9.2 mg., the phosphorus 2.8 mg., and the alkaline phosphatase 5.8 Bodansky units per 100 cc. The blood Hinton reaction was negative. The urine was acid, with a specific gravity of 1.014, a slight trace of albumin and a moderate amount of sugar. The urinary sediment was negative. The stool gave a ++ guaiac reaction.

The hospital course was one of progressive decline. The diabetes was easily controlled, but the patient continued to suffer from left-upper-quadrant pain and anorexia. He was given therapeutic doses of sulfathiazole. He gradually became weaker and incontinent, and died on the 27th day after admission.

Autopsy (A-41-423). The body was that of a normally developed but rather emaciated man. External examination revealed nothing of note. There was 150 cc. of fibrinopurulent exudate in the peritoneal cavity, and the peritoneal surfaces were covered by similar exudate. The lower surface of the liver, both kidneys and adrenal glands, spleen and pancreas all formed part of a large mass bound together by fibrinopurulent material. In the lesser peritoneal cavity and extending retroperitoneally was a large abscess containing foul brown pus. The duodenum formed one wall of this abscess, but the lumen was not affected. The celiac and superior mesenteric arteries contained large friable thrombi almost completely filling their lumens. The splenic vein was completely occluded by a friable necrotic clot, together with considerable purulent material. The portal vein showed thrombosis and purulent matter, which could be traced into the parenchyma of the liver.

The liver weighed 2030 gm. The capsule was intact. The surface and parenchyma were deep red, spotted by many irregular, pale yellow gray areas, which measured from 0.2 to 5.0 cm. in diameter. The centers of many of these areas were soft and necrotic and filled by creamy yellow mucopurulent material. It was estimated that these pale areas occupied two thirds of the liver substance. Microscopically, sections from the liver showed many abscesses, with necrotic liver cells, polymorphonuclear leukocytes and bacilli. The majority of the abscesses appeared to originate in the portal spaces. The walls of the abscesses showed marked polymorphonuclear leukocytic infiltration.

The portal vein was lined by an organizing, centrally liquefied thrombus. There was diffuse polymorphonuclear leukocytic infiltration of the vessel wall and surrounding tissue. A section taken from the splenic vein showed essentially the same process.

The wall of the gall bladder was markedly thickened by fibrous tissue and averaged 0.8 cm. in width. At the fundus was a large pocket of pus, which was walled off from the lumen. The lumen of the gall bladder contained pale, mucoid, slightly purulent bile. There was diffuse lymphocytic infiltration of the wall. Throughout the wall were focal masses of polymorphonuclear leukocytes. The walls of the cystic and common ducts were thickened and contained pale bile similar to that in the gall bladder.

The pancreas was soft and friable, and contained many irregular, rough stones averaging 0.2 to 0.6 cm. in di-

ameter. Most of these stones were surrounded by brown pus and were contained in small cystic spaces.

Sections from the pancreas showed a large portion of the parenchyma to be replaced by masses of polymorphous nuclear leukocytes or diffusely infiltrated by lymphocytes and fatty macrophages. One section showed proliferation of atypical duct epithelium growing in a definitely circumscribed nodular arrangement. However the tumor was growing along a nerve sheath in one area. This was interpreted as an early adenocarcinoma of the head of the pancreas.

In addition to the above lesions, there were a chronic gastric ulcer and healed focal pyelonephritis.

K. pneumoniae was cultured from the heart's blood, the liver abscesses, the gall bladder and the peritoneal abscess. It reacted with Type A serum.

CASE 7. P. K. (BCH 1,033,118), a 71-year-old man, was admitted in a semistuporous condition on July 19, 1941. Three weeks previously, he experienced a sudden onset of vague upper abdominal pain, which persisted for 1 day. The pain was accompanied by a temperature of 101°F and was followed by slight jaundice which disappeared after 2 days. The patient was treated with sulfanilamide and digitalis. The pulse and temperature became normal, the sulfanilamide was omitted but the digitalis was continued. The patient remained drowsy, however, and the only complaint was that of difficulty in urinating. On the evening before entry, he had a shaking chill and the temperature rose to 103°F. The past history was irrelevant.

At the time of admission, the temperature was 97.8°F, the pulse 80, and the respirations 20. The blood pressure was 110/54. Physical examination revealed a very acutely ill, well-nourished, stuporous man. The trachea was deviated to the left, and there was marked limitation of expansion of the entire left chest over the same area; there were dullness to flatness, diminished breath sounds and diminished tactile fremitus. The heart sounds were distant, and the cardiac rhythm was regular. There was a short, rough, systolic apical murmur transmitted to the axilla and base. The abdomen was soft and rounded. A sharp, firm, nontender liver edge was felt 3 cm below the right costal margin. There was no tenderness or spasm. The prostate was symmetrical, movable moderately enlarged and nontender. The remainder of the physical examination was negative.

Examination of the urine revealed specific gravities varying between 1.006 and 1.020, a mild albuminuria and persistent moderate pyuria. Urine cultures consistently showed *K. pneumoniae*, *Esch. coli* and enterococci. Examination of the blood showed a red cell count of 2,900,000 with a hemoglobin of 62 per cent (Sahli), and a white-cell count of 16,000 with 53 per cent polymorphonuclear leukocytes, 36 per cent band forms, 2 per cent metamyelocytes, 1 per cent myelocytes, 1 per cent basophils, 3 to 5 per cent lymphocytes and 3 to 5 per cent monocytes. The mean corpuscular volume was 107 cu microns, the mean corpuscular hemoglobin concentration 31 per cent, and the mean corpuscular hemoglobin 33 microgm. The blood Hinton reaction was negative. The total serum protein was 5.6 gm per 100 cc, with an albumin/globulin ratio of 1.0. The icteric index was 3. The formal gel test was weakly positive. A bromsulphalein test showed 70 per cent retention of the dye in 5 minutes and 20 per cent in 15 minutes. The prothrombin time was normal and urobilinogen was present in the urine in a 1:2 dilution. Blood culture revealed no growth.

Gastric analysis showed 32 units of free acid before and 92 units 1 hour later. The fluid was guaiac negative. Guaiac tests of the stools were repeatedly negative.

A roentgen study of the chest was negative. A gastrointestinal series was interpreted as showing an old duodenal ulcer, with perigastrophic adhesions and a hiatus hernia. A spot film of the gall bladder showed no evidence of gall stones. Two barium enema studies were unsatisfactory.

The patient remained semistuporous throughout his hospital stay. During the 1st week, he had three shivering chills, the temperature spiking from 102 to 103°F. Sulfadiazine therapy was instituted, and blood concentrations reaching 10 mg per 100 cc were attained. During the 2nd week the patient was afebrile, and sulfadiazine was omitted. During the ensuing 3 weeks he had intermittent low grade fever. Accordingly, sulfadiazine was started again and continued for about 2 weeks, after which, because of continued fever, sulfathiazole was substituted and continued until the patient's death. The laboratory and physical findings remained essentially unchanged during the final 2 days in the hospital; the patient began to vomit and became comatose. The nonprotein nitrogen rose to 83 mg and the sulfathiazole level to 21 mg per 100 cc, and the patient died quietly at the end of the 10th week in the hospital.

Autopsy (A 41,643). External examination of the body revealed nothing of note. The liver weighed 1600 gm. The capsule was smooth and glistening, and through it could be seen small, irregular areas, lighter in color. On section, numerous abscesses ranging from 2.5 to 5.0 cm in diameter were seen throughout the right quadrate and caudate lobes. These abscesses were filled with a greenish yellow, thick, tenacious exudate with a glairy appearance. The walls of the abscesses were irregular and contained fibrous connective tissue microscopically. The walls of the abscesses were diffusely infiltrated by polymorphous clear leukocytes, and many bacilli were present. Patchy cholangitis of the small ducts and a slight degree of old biliary cirrhosis were noted. The gall bladder was small and almost entirely embedded in the liver substance. The walls were thickened to 4 mm and, microscopically, were found to be studded with minute intramural abscesses. The lumen contained numerous faceted pigment calculi measuring up to 3 cm in diameter, which were bathed in an exudate similar to that found in the liver abscesses. The common bile duct, which was slightly dilated, contained bile but no calculi. The portal vein showed no evidence of phlebitis.

There was no evidence of inflammation about the appendix or the numerous diverticula of the sigmoid colon. The spleen weighed 60 gm and was normal. The kidneys showed a slight amount of chronic pyelonephritis and retention of sulfathiazole crystals in the pelvis. The prostate contained active infection and at least one healing abscess. Unfortunately, no culture was taken. There were moderate edema and congestion of the lungs. The heart was negative. The vertebral bone was quite fatty and hypoplastic.

No organisms were cultured from the heart's blood. *K. pneumoniae* was cultured from the liver, the liver abscesses and the gall bladder, the strain reacted with Type B serum.

DISCUSSION

A careful study was made of the clinical histories, signs and symptoms of our cases and of

those reported in the literature. No single sign or symptom was found that would distinguish liver abscess due to *K. pneumoniae* from those in which the usual pyogenic organisms were the etiologic agents.

The only laboratory finding of value in the diagnosis of liver abscess due to *K. pneumoniae* was the blood culture, which was positive in 11 of 23 cases reported in the literature. In the cases reported above, ante-mortem blood cultures were taken in 6, and *K. pneumoniae* was recovered in 1.

Pathology

The gross appearance of the liver abscess due to *K. pneumoniae* is, except for the exudate, similar to that in abscesses caused by other pyogenic organisms. In all but 1 of the cases presented above, there was multiple abscess formation. Of the 23 cases in the literature, the livers in 2 contained a single abscess. Two abscesses were found in one case, and three in another, whereas the livers of the remaining cases showed multiple abscess formation.

The exudate in all the cases presented above was characteristically glairy and mucoid. The exudate appears similar in all respects to that seen in *K. pneumoniae* infections of other parts of the body.

Microscopically, there is nothing to distinguish these abscesses from other pyogenic liver abscesses except for the finding of organisms with the morphology of *K. pneumoniae*.

Disease of the biliary system other than the liver was present in 4 of the 7 cases in the present series, in only one of which (Case 5) there was definite obstruction of the common bile duct; another (Case 6) was associated with acute suppurative cholecystitis and cholelithiasis, acute suppurative pancreatitis, early adenocarcinoma of the head of the pancreas and acute pyelophlebitis. Case 7 was associated with acute empyema of the gall bladder, with cholelithiasis but no infection of any of the hepatic bile ducts. Case 3 was associated with chronic cholecystitis with cholelithiasis. In Case 2, the abscess resulted from direct extension from the stomach. It appears from this small series of cases that the pathogenesis of liver abscesses due to *K. pneumoniae* is varied and is similar to that of other pyogenic liver abscesses. In Cases 1 and 4, there was no associated biliary, gastrointestinal or urinary-tract infection.

Only 15 cases were found in the literature with reports complete enough to allow consideration of etiologic factors. Ten were associated with extra-hepatic biliary disease. Of the remaining 5 cases, 1 was complicated by bronchopneumonia and empyema due to *K. pneumoniae*; 1 followed acute

appendicitis, and 1 was associated with bronchiectasis and lung abscess from which Friedländer's bacillus was cultured. In the other 2 cases, no definite source of infection could be determined.

Bacteriology

Until recent years, *K. pneumoniae* has been associated in the minds of most observers as occurring primarily in the upper respiratory tract. This undoubtedly is largely because Friedländer,¹² in first describing the organism in 1882, named it the pneumobacillus and regarded it as the etiologic agent in lobar pneumonia. Even after Weichselbaum¹³ demonstrated that the pneumococcus was the cause of lobar pneumonia, *K. pneumoniae* was always considered the agent responsible for a particularly malignant type of lobar pneumonia. Very little attention was given to the organism as an infective agent in other parts of the body, although numerous reports described the bacillus as causing suppurative lesions in practically every organ of the body. It has also been described as occurring in many domestic animals.

In 1937, Baehr, Schwartzman and Greenspan⁸ reported a study of 198 cases of infection with Friedländer's bacillus. In this series, there were 25 cases of lung or upper-respiratory-tract infection, only 2 of which were cases of pneumonia in which the clinical and bacteriologic evidence indicated that *K. pneumoniae* was the primary cause of pneumonia. In 7 other cases of pneumonia, the authors recovered this organism in association with the pneumococcus or streptococcus. It is the experience of this laboratory that Friedländer's bacillus usually occurs as a secondary invader rather than as the primary organism in cases of lobar pneumonia and bronchopneumonia. In the series of Baehr, Schwartzman and Greenspan, the bacillus occurred in the gastrointestinal tract in 61 cases, in the genitourinary tract in 56, and in the biliary system and liver in 46.

It has been pointed out by Dudgeon¹⁴ and Kendall¹⁵ that the Friedländer bacillus is often found as a normal inhabitant of the intestinal tract.

The cultural and morphologic characteristics of the Friedländer bacillus are well known and need not be described here. However, comparatively little attention has been given to the type specificity of the various strains of this organism and to their clinical significance. Many unsuccessful attempts have been made by various investigators to arrive at a satisfactory classification of the Friedländer group by fermentation of the sugars. It was not until Julianelle,¹⁶ in 1926, developed a serologic classification that any order was brought to this group. He found that there are three sharply defined and specific types and one heterogeneous

group of *K. pneumoniae*, and that the agglutination, agglutinin adsorption, protection, thread and precipitin reactions are highly specific for each type. Edwards,¹⁷ who was able to confirm the work of Julianelle, demonstrated only two serologic types; a Type 1, which was mainly of equine origin and corresponded to Julianelle's Type B, and a Type 2, which was of human origin and corresponded to Julianelle's Type A.

Julianelle¹⁸ carried out further work in which he studied eighty strains of *K. pneumoniae* gathered from various sources. He found 52 per cent to be Type A, 15 per cent Type B, 9 per cent of Type C and 24 per cent Group X. Type A, for the most part, consisted of strains derived from man, and more than 70 per cent of these were associated with pneumonia in human beings. The greatest number of Type B strains came from animal sources. The strains from heterogeneous Group X were found in a great variety of diseases.

Before the serologic typing of the organisms in the cases presented is discussed, it should be pointed out that Type A serum has been available here only since 1939, whereas Type B serum was first obtained by this laboratory in 1940. To date, Types C and X serums have not been obtainable.

Of the 7 cases presented above, the organism in only 1 case (Case 6) reacted with Type A serum. This is of particular significance, because this type, in the experience of this laboratory, is usually associated with respiratory infections. According to Perlman and Bullock,¹⁹ of 37 cases of Friedländer pneumonia, 29 were caused by Type A and only 8 were caused by Type B. Solomon^{20,21} reported similar results: in 9 cases of chronic Friedländer pneumonia, 7 were caused by the Type A strain, 1 by the Type B and 1 by the Type C; and in 10 cases of acute Friedländer's pneumonia all were caused by the Type A strain.

The organism in Case 7 belonged to Type B. Again, there were no lung lesions and the blood culture was negative.

The bacilli from Cases 2, 3 and 4 were not reacted on by the Type A serum, and therefore belong to Type B or C or Group X, whereas the capsules of the organisms in Case 5 did not swell in the presence of either Type A or B serum. The patient in Case 1 was autopsied before any serum was available, and thus the organism was not serologically typed. However, it was not a lactose-fermenting organism, and it has been the experience in this laboratory that the Type A organisms are lactose fermenters.

Recently, a case of common-duct obstruction with pericholangitis and empyema of the gall bladder came to autopsy. Friedländer's bacillus was

cultured from the liver and the gall bladder. This organism was not reacted on by either the Type A or the Type B serum.

To summarize, 1 case of biliary tract infection was infected with the Type A organism, whereas 6 were definitely not. To this group, the case that was not typed could in all probability be added. Of these 7 cases, 3 are known definitely not to belong to Type B. Although the number of cases presented is too small to draw definite conclusions, it is interesting to draw attention to the large preponderance of organisms other than those classified as Type A in these hepatic infections.

SUMMARY

Seven cases of liver abscess due to *Klebsiella pneumoniae* (Friedländer's bacillus) are reported, and the autopsy and bacteriologic findings are discussed. One case of empyema of the gall bladder and cholangitis due to Friedländer's bacillus is mentioned.

The significance of the serologic typing of Friedländer's bacillus is discussed. In the cases presented, all but one of the organisms belonged to serologic groups other than Type A.

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THE FAILURE OF COBRA VENOM TO RELIEVE PAIN IN RHEUMATOID ARTHRITIS*

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PAIN is the greatest single factor responsible for restricted joint motion, subsequent muscle atrophy and articular deformity in rheumatoid arthritis. The course and outcome of this disease would presumably be more favorable if pain could be completely controlled. Unfortunately there is no analgesic capable of producing such an ideal situation, although the salicylates, especially acetylsalicylic acid (aspirin), administered in maximal dosage most nearly approach this goal.

The use of cobra venom was suggested by reports of its analgesic action not only in cancer¹⁻³ but also in various rheumatic diseases.^{2, 4} Macht¹ attributes its effect in human beings to a central action on the higher cerebral nerve centers. In comparison with morphine it is supposed to produce a more delayed but longer-lasting analgesia.

Moderate success has already been claimed for its use in arthritis. Although Macht² thought that the 10 arthritis patients treated by him formed too small a group to warrant discussion, he noted that "considerable relief of pain has been obtained in some instances." Steinbrocker and his associates⁴ reported that 11 of 13 patients with rheumatoid arthritis experienced slight to moderate improvement. Varying degrees of benefit were observed in other patients with degenerative joint disease, so-called "fibrositis" and "neuralgia." The reports of Burkhardt,⁵ who used intracutaneous injections of venoms from *Vipera aspis* and *Vipera ammodytes*, and that of Butler,⁶ who administered copperhead venom intradermally, are not sufficiently detailed to allow evaluation of their results. Because of the need of a more ideal analgesic in rheumatoid arthritis it has seemed advisable to attempt to corroborate the reports.

METHOD

Availability and the preliminary criteria for the selection of questionable clinical, laboratory and roentgenologic cases of rheumatoid arthritis. The patients, however, had no previous control, having

been treated for pain were the patients with uncontroverted x-ray evidence of disease. The patient served as his own control. The patient served for seven

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months to several years before treatment. All were followed subsequently for four weeks to six months. Nine were hospitalized and on bed rest during the period of therapy; three were ambulatory, having been hospitalized previously. Physiotherapy and necessary orthopedic measures were continued, but acetylsalicylic acid was omitted in all but 1 case. All patients were seen daily by the same observer and evidence of objective as well as subjective improvement was noted. Measurements of pain thresholds were made in 4 patients. Laboratory data relative to blood cytology, urinalyses and corrected sedimentation rates⁷ were obtained in all cases.

Cobra venom§ was administered intramuscularly each day. Larger doses were employed than had been used by Macht¹ (5 mouse units daily until relief of pain was noted) and Steinbrocker et al.⁴ (10 mouse units daily to a total dosage of 50 units before considering the result a failure). Our first 2 patients received 10 units daily for four to six days, then 20 units a day for three to four days, and eventually 30 units every twenty-four hours. All other patients were given 10, 20 and 30 mouse units on each of the succeeding first three days and 30 units daily thereafter. A total of at least 300 mouse units was given in all cases, a dosage adequate to demonstrate any analgesic action of cobra venom.

RESULTS

The data of the individual cases are shown in Table 1.

Toxicity

No serious toxic effects were noted with the large doses employed. In Case 2, the patient experienced a transitory sedative effect on several occasions. Local reaction at the site of injection occurred in only 1 patient (Case 12). In this case, twenty minutes after each injection there appeared an irregular erythematous area, 2 cm. in diameter which was accompanied by local heat. There was marked local pain for five to twelve hours. After twenty-four hours a 1-cm. ecchymotic, slightly elevated, warm induration persisted, which slowly disappeared in the course of several days.

*Dr. David I. Macht of Hynson, Westcott and Dunning, Incorporated, Baltimore, Maryland, kindly supplied the cobra venom used in this study. The preparation contained 10 mouse units per cubic centimeter of solution.

CASE NO.	PATIENT	SEX	AGE	DURATION OF DISEASE	STABILITY OF DISEASE	PREVIOUS TREATMENT AND EFFECT	STATE OF DISSEMINATION	X-RAY FINDINGS	SEMIQUANTITATIVE RATE	TOTAL DOSE OF ACETYL-SALICYLIC ACID	ANALGESIC EFFECT OF COBRA VENOM	REMARKS	
									BEFORE THERAPY	AFTER THERAPY	COBRA VENOM		
									mm / min	mm / min	mm / min		
1	G. L. (No 18146)	M	26	4	Marked progress since	Hospitalization, outpatient measures, theophylline and Relaxin with temporary benefit	Exacerbation increased pain	Osteoporosis of spine, fusion of sacrospinous joints, narrowing of hips	0.46	0.52	345	Good	Hip pain increased while taking cobra venom, no objective changes, acetylsalicylic acid far superior
2	S. K. (No 00132)	M	22	8	Marked progress since (2 yr), in bed (1 yr)	Hospitalization and outpatient measures with slight benefit	Active constant pain in all joints	Narrowing of joint spaces with bony fusion in some	1.54	1.67	355	Poor	Less pain and stiffness noted after 175 units, no objective changes. Patient evaluated 50-75 per cent relief of pain occasionally felt sleep after an injection
3	A. B. (No 157841)	M	55	5	Marked progress since	Hospitalization, vitamin D, cobra venom and Relaxin (2 courses) with no benefit	Active constant pain in all joints	Irregular narrowing and destruction of wrists, hands and elbows	1.92	Not done	395	Poor	No subjective or objective change
4	M. V. (No 220589)	F	29	13	Moderate remission with pregnancy lasting 3 yr	None	Active exacerbation for 8 months moderate pain	Destructive changes of joint margins of some interphalangeal joints	0.74	0.72	440	Good	Claimed 25-50 per cent relief of pain, starting after 175 units, no objective changes as good results with acetylsalicylic acid
5	H. H. (No 127252)	F	49	10	Moderate remission in part for 5 yr	None	Active exacerbation, moderate pain in some joints	Decalcification of metacarpals and bony destruction of some	1.23	1.58	300	Fairly good	No relief of pain, acetylsalicylic acid superior
6	E. A. (No 327707)	F	40	3½	Moderate	None	Moderately severe pain in all joints	Destruction of some interphalangeal joints	0.91	0.86	300	Good	No relief of pain, acetylsalicylic acid superior
7	A. B. (No 321644)	F	53	2½	Marked progress since	Serum injections with no benefit	Active severe pain in all joints	Widened joint spaces, narrowing of many joints	1.25	1.1	300	Good	Increased pain while taking cobra venom, acetylsalicylic acid far superior
8	P. A. (No 150155) ambulatory	M	40	5½	Moderate	Hospitalization and outpatient measures with slight benefit	Mildly active in dermis, pain	Narrowing of left wrist and scapulothoracic joints	0.33	Not done	300	Fair	Increase in pain to point of incapacitation while taking cobra venom, acetylsalicylic acid far superior
9	H. N. (No 148322) ambulatory	F	29	10	Mild several remissions	Hospitalization, physiotherapy, and outpatient measures with moderate benefit	Mildly active with objective changes	New bone formation about scrotothoracic joints	0.36	0.17	300	Poor	Less constant back pain after 180 units return of condition, worse in 36 hr after medication stopped, better than acetylsalicylic acid
10	C. N. (No 09771) ambulatory	M	51	8	Moderate remission in part	Hospitalization with no benefit	Active exacerbation increased pain and marked functional symptoms	Decalcification of tarsal and carpal bones	1.57	1.63	300	Good	No benefit from cobra venom, unable to do without acetylsalicylic acid at any time
11	G. M. (No 170093)	F	62	7	Moderate progressive	Symptoms both knees and sold with moderate benefit	Active exacerbation with severe pain and arthritis	Decalcification of metacarpals and feet	1.53	1.42	300	Good	Increased pain during treatment, and joint motions more restricted
12	C. O. H. (No 34533)	F	37	10	Moderate slowly progressive remission in part with pregnancy	None	Active exacerbation 1 yr moderate pain	Narrowing of joint spaces some joint destruction in hands, wrists and feet	0.61	0.38	300	Good	Increased pain while taking cobra venom, local treatment of injection frequently requested acetylsalicylic acid for relief

Subjective Improvement

Three of the 12 patients (Cases 2, 4 and 9) experienced some degree of subjective improvement. In Case 2 the patient claimed 50 to 75 per cent relief, manifested by decrease in pain and stiffness, first noted after the administration of a total of 175 units. He considered the effect superior to that of acetylsalicylic acid. In Case 4 the patient admitted 25 to 50 per cent relief of pain, apparent after a total dose of 175 units, but stated that aspirin was equally effective. Both these patients were treated during exacerbations of the disease and had almost constant pain and stiffness. In Case 9, an ambulatory patient in a partial remission experienced about 50 per cent relief based on inconstancy rather than decreased intensity of pain after receiving 180 units. Acetylsalicylic acid was regarded by her as inferior. The prolonged analgesic effect attributed to cobra venom was not observed, since her symptoms increased within thirty-six hours after the drug was discontinued.

All nine of the remaining patients experienced either no relief or an actual increase in the amount of pain and stiffness, possibly owing to the withdrawal of acetylsalicylic acid. They invariably believed the latter to be a superior analgesic.

Objective Improvement

Reduction of articular swelling or effusion or increase in muscle strength or range of joint motion was not observed in a single individual. An attempt was made in Cases 1, 2, 3 and 4 to measure objectively the effect of cobra venom on pain threshold in order to note any correlation with subjective improvement. A modification⁸ of the method of Hardy, Wolff and Goodell⁹ was used, consisting essentially of determining the threshold for the pain produced by thermal radiation of the skin.* The relation between pain elicited in the skin by thermal radiation and that arising from a diseased joint is not established. However, the measurement employed offers the most satisfactory method available for obtaining objective evidence of reduced sensitivity to pain.

In Case 1, nine determinations were made before and during treatment. All results remained within the normal range expected for race and age. This agreed with the clinical response. One patient (Case 2), who derived the greatest benefit subjectively, showed an extremely high threshold of pain at first, but no change in eight subsequent tests during treatment. The lack of subjective relief in Case 3 coincided with the lack of alteration

of pain threshold even after a total dose of 375 units. Subjective improvement in Case 4 was first admitted after 175 units. However, it was not until a total of 440 units had been given that it became possible to discern an appreciable elevation in pain threshold as objective evidence of relative hypoactivity.

Although the results of this study indicated a slight correlation between subjective and objective findings, the number of patients was too small to permit definite conclusions.

Laboratory Studies

No striking effect on the sedimentation rate was noted. In one patient (Case 2) who showed subjective improvement the rate rose from 1.54 to 1.67 mm. per minute, whereas another (Case 12), who had increased symptoms during treatment, showed a fall in the sedimentation rate from 0.61 to 0.38 mm. There were no appreciable changes in erythrocyte and leukocyte counts or hemoglobin content. Urinalyses did not deviate from normal. Neither febrile nor antipyretic effects were observed as a result of the venom.

SUMMARY

The effects observed with large doses of cobra venom for the control of pain in rheumatoid arthritis were disappointing and contrary to previous reports. Three of 12 patients experienced subjective relief, estimated variably from 25 to 75 per cent. In no case was improvement complete, dramatic or lasting. There were no objective alterations. The only significant toxic effect was local reaction at the site of injection in 1 patient. Acetylsalicylic acid was considered to be as good or better as an analgesic by 10 of the 12 patients studied.

The results indicate that cobra venom is of no value for the relief of pain associated with rheumatoid arthritis.

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*We are indebted to Dr. William Chapman for performing these experiments.

METHYL SALICYLATE POISONING

A Report of Five Cases

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THE danger of poisoning by oil of wintergreen has not been sufficiently emphasized. It is commonly used in the home, and may be accidentally ingested by children, who, as Shipley¹ points out, may associate the pleasant aroma with wintergreen-flavored candy. It is therefore wise to continue the reporting of such cases. I present a brief summary of the cases reported to date, and 5 additional cases, 2 of which were seen by me.

Lawson and Kaiser² in 1937 tabulated 43 cases from the literature and added 1 of their own. In the same year Stevenson³ gathered 45 reported cases, 10 of which were not included in Lawson and Kaiser's summary, and added 3 of his own—making a total of 57. Not included by either author were 4 cases reported by Shipley¹ in 1933, and 1 case reported by Bowen, Roufa and Clinger⁴ in 1936. In 1938, Kane⁵ reported 2 cases, Eimas⁶ 1 case, and Baxter, Hartwell and Reck⁷ 2 cases. Donatelli and Abbate⁸ reported 1 case in 1939, Shurreff and Pearlman⁹ 2 cases in 1940, and Epstein and Work¹⁰ 1 case in 1942. To this final total of 71 reported cases are added the 5 additional cases described below.

Thirty seven of these 76 patients died. Twenty-three of the fatal cases occurred in children under five years of age. The smallest fatal doses were estimated at 4 cc. for a child one and a half years of age,² and 4 cc. for a two year-old child.³ A number of small children died from slightly larger doses. One death in a two-and-a-half-year old child following the external administration of methyl salicylate was reported by Lawson and Kaiser.² The smallest fatal dose reported in an adult was 6 cc.¹¹ The largest estimated doses followed by recovery were 30 cc. for a child two years of age, and 30 cc. for several adults.^{2,8} However, dosage reports, even as estimates, are obviously only partially reliable, particularly in small children.

The usual more severe course involves vomiting, hyperpnea, diaphoresis, extreme thirst, dehydration, stupor and convulsions. In the fatal cases death commonly occurs within twenty four hours. Kane⁵ reported a patient who died two and a quarter hours after ingestion of the poison. The commoner pathological findings observed at autopsy in cases of methyl salicylate poisoning^{11,12} include acute degenerative nephritis, edema and

fatty degeneration of the liver, congestion and edema of the lungs, acute gastritis and hyperplasia of the lymphoid structures in the intestinal tract, and small hemorrhages in the pericardial membrane and the pleurae and subdurally. Dodd, Minot and Arena¹³ have studied the altered physiology in salicylate poisoning in general, and have discussed treatment rationale, including the necessity for administering large amounts of fluid and combating acidosis.

The 5 additional cases are as follows:

CASE REPORTS

CASE 1. A 2 year old boy was brought to the office about 4 hours after having swallowed an estimated 15 cc of methyl salicylate, this was followed by vomiting and alternate periods of restlessness and mild stupor. The chief features on his arrival were marked perspiration, rapid breathing and pale mucous membranes. Vomiting was mechanically induced. Following this procedure, a Levin tube was introduced and the stomach was thoroughly irrigated with a dilute solution of sodium bicarbonate. A definite oil of wintergreen odor was obtained from the aspirated fluid. The lavage was continued for a long period of time, until finally no odor of the drug could be detected. The patient was then sent to the hospital with a guarded prognosis.

Treatment at the hospital consisted chiefly in forcing fluids by mouth, including dilute solutions of sodium bicarbonate. Significant laboratory findings were acetone, diacetic acid and a trace of albumin in the urine and a white cell count of 20,000. The child's symptoms and the urinary findings subsided fairly promptly. He was discharged home in good condition on the 3rd day.

CASE 2. A 55 year old man was seen about 6 hours after having ingested one tablespoonful (15 cc) of methyl salicylate for "heartburn." He was unaware of the toxicity of the drug for internal use. One hour after ingestion, the patient developed uninitus, "a full head" and numbness of the upper and lower extremities. Two hours later he became hot, perspired freely and breathed rapidly. Because of intractable gagging with attempted use of the nasal tube, an automatic lavage was employed by having the patient drink huge quantities of a dilute solution of sodium bicarbonate, with consequent induction of vomiting. A strong oil of wintergreen odor was present in the vomitus. The treatment was continued for an extended period of time, until finally no odor could be detected. After vomiting, the patient stated that he felt better immediately and that the numbness had greatly decreased. The patient had no sequelae except for a transitory albuminuria.

Two urine specimens produced slight reduction of Benedict's solution, but the patient failed to co-operate with requests for further checking. It therefore is not

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known whether the copper reduction was the result of the salicylate or of a mild underlying glycosuria.

CASE 3.* A 2-year-old girl was seen in her home about 6 hours after she had ingested methyl salicylate. An estimated ounce (30 cc.) was missing from a bottle containing synthetic oil of wintergreen, but some had been spilled. An oil-of-wintergreen odor was present on the child's breath. There were rapid breathing and restlessness. The child was hospitalized.

In the hospital, hyperpnea was marked, the pulse was rapid, and pallor was present. The patient's condition appeared to become serious, and she was alternately listless and restless. Treatment consisted chiefly in stomach lavage, sodium bicarbonate medication and repeated saline hypodermoclyses. The patient showed improvement after 15 hours of treatment, and was well enough to be discharged home on the 3rd day.

CASE 4† A child about 3 years old was seen in the accident room of the Cambridge City Hospital about ½ hour after the ingestion of oil of wintergreen. About one quarter of an ounce (7.5 cc.) was missing from the bottle, but some had been spilled. The patient vomited profusely, and further vomiting was then induced. As the patient did not appear ill, he was sent home without further treatment. About ½ hour later convulsions occurred, to which, however, the patient was said to be subject. Arrangements were made for immediate return to the hospital, but on arrival the patient was dead. Death had occurred within 2 hours after the taking of the poison.

CASE 5‡ A 48-year-old woman was admitted to the Cambridge City Hospital 2 hours after having taken one teaspoonful (4 cc.) of methyl salicylate by mistake. She had vomited shortly afterward, noted ringing of the ears and felt nauseated. On entry, the patient's stomach was lavaged, and later 2000 cc. of 5 per cent glucose solution was given by clysis. No further toxic symptoms developed. The urinary findings were negative except for an "orange" copper reduction, which could have been due to the glucose medication. The patient was discharged home recovered on the 7th day.

DISCUSSION

The toxicity of oil of wintergreen should be more widely appreciated. Its poisonous nature when ingested should be stressed in medical schools, and among physicians and the laity. Bottles containing methyl salicylate should bear poison labels and be kept safely out of reach of children.

*Reported through the courtesy of Dr. John J. McLaughlin of Albany, New York.

†Reported through the courtesy of Dr. Robert F. Ober, of Brookline, Massachusetts.

Cases 1, 2 and 5 suggest the value of prompt and thorough lavage. This procedure may very well have been the chief reason for the mild courses that followed. Lavage and the copious administration of parenteral fluids in Case 3 presumably aided in the recovery of this more seriously afflicted patient.

Treatment to rid the stomach of the poison must be adequate. Mere vomiting may induce a false sense of security. Indeed, more than one child has died after a parent has been told that its vomiting precluded the necessity for further treatment. Ordinary vomiting does not completely remove methyl salicylate from the stomach. Gastric lavage should be done when the patient is first seen, and should be prolonged until no trace of the drug odor is present in the washings. If the tube is not tolerated, an automatic lavage should be employed: that is the patient should be forced to drink huge quantities of water or of a dilute solution of sodium bicarbonate, with consequent induction of vomiting. To be adequate the process must be repeated again and again.

SUMMARY

The toxicity of methyl salicylate is emphasized, and proper treatment following its ingestion is discussed.

Five such cases of poisoning are reported.

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MEDICAL PROGRESS

HEMATOLOGY*

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DURING 1942, relatively little that is new or startling in the hematological field has occurred. Further developments with reference to the Rh factor and its relation to erythroblastosis foetalis have taken place; much has been written of transfusions, plasma and transfusion reactions; the hemolytic syndromes continue to occupy a prominent place; and the hemorrhagic states have received much attention. Leukemia remains as much of a problem as heretofore despite an initial flurry of enthusiasm for radio-phosphorus.

BLOOD CELLS

The matter of *elliptic erythrocytes* and *elliptocytosis* has been studied by Wyandt, Bancroft and Winship.¹ Eighty-six new cases in three large families of German extraction are reported. In all except 1 case, in which there was an associated spherocytosis, no anemia or other abnormality was present, and the condition was apparently without significance. All vertebrate animals with the exception of mammals have elliptic and nucleated red cells. The further exception to the latter statement is the camel, which has elliptic, non-nucleated red cells. It is probable that elliptocytosis is commoner than is generally recognized. This abnormality should not be confused with the elliptocytosis occurring in connection with the target cell and increased hypotonic resistance, noted chiefly in persons of Italian and Greek origin. There is a large group of syndromes affecting Mediterranean peoples, chiefly Italians, which is characterized in part by the presence of abnormally thin, hypotonically resistant target cells (so-called "leptocytes") and elliptocytes.² These disorders are inherited as a Mendelian dominant and vary in severity from the fatal Cooley's anemia to very mild conditions of no significance to the individual himself, but important from the hereditary standpoint.

The *target cell*, as noted in previous reviews, is assuming greater importance as it is realized that from the standpoint of thickness, three types of red cells can be discriminated: the normocyte, approx-

imately 2.0 microns thick; the spherocyte, 2.5 to 3.5 microns thick; and the leptocyte, approximately 1.5 to 1.7 microns thick. The thicker the red cell, the more fragile it is to hypotonic salt solutions. The leptocyte is thus the antithesis of the spherocyte. Of interest is the fact that the former cell is present in large numbers in sickle-cell anemia. It is possible that the target cell, the oval cell and the sickle cell—when they are inherited—are more or less related. The target cell may occur, as Bohrod³ has pointed out, shortly after hemorrhage; there it probably represents a relatively thin and somewhat younger red cell. To assume, as Bohrod does from the findings after hemorrhage, that the target cell is always simply a hyper-resistant young cell that appears in the blood following active bone-marrow regeneration seems illogical, since it is commonly found in persons without evidence either of blood loss or of increased blood destruction. In another paper, Bohrod⁴ points to an increasing resistance of the bowl-shaped target cell to dilute acetic acid.

Schleicher⁵ discusses at length the origin and nature of the *Cabot ring bodies* in erythrocytes. Although most authorities have considered them to be of nuclear origin, Schleicher presents evidence that they are actually the expression of a denatured or colloid protein connected with the nucleus and produced by the activity of a lysin on the lipoprotein constituents of the red cell.

The exact nature of the *eosinophil* remains obscure. It is certainly a granulocyte and thus a bone-marrow cell. However, its behavior with respect to pathologic processes differs strikingly from that of the neutrophilic granulocyte. Thus in acute pyogenic infections, with a sharp increase in polymorphonuclear neutrophils, the eosinophils drop out of the picture, whereas with subsidence of the infection they increase in number. Thus the eosinophil seems to have a reciprocal relation to the neutrophil. Why it becomes increased in allergic conditions and in such widely separated entities as parasitic infestation and periarteritis nodosa is not known. The stimulus that provokes the production and delivery of eosinophils to various parts of the body, and thus eosinophilia, is as yet obscure. An unusual, although by now well-documented, type of eosinophilia is that described by Loeffler of Switzerland in 1936 and often known as *Loef-*

*Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual*, Vol. III, 1942 (Springfield, Illinois: Charles C. Thomas Company, 1942, \$5.00).

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fler's syndrome. This is characterized by a transient and rapidly shifting infiltration of the lungs, and is accompanied by relatively few symptoms, indicating a mild infectious process. Eosinophilia of 15 to 35 per cent, occasionally higher, is present. Neither the nature of the infection nor the cause of the eosinophilia has been determined. Elsom and Ingelfinger⁶ report a probably related, if not identical, entity in 2 cases of eosinophilia and pneumonitis in chronic brucellosis. Both cases showed well-defined eosinophilia up to 42 per cent, peculiar pulmonary lesions and rather definite evidence of brucellosis. The cases known as Loeffler's syndrome were not studied for the question of undulant fever, and it is possible that both Elsom and Ingelfinger's cases and those of Loeffler and others may be peculiar examples of brucellosis with involvement of the lungs and with eosinophilia.

Infectious mononucleosis continues to present interesting diagnostic possibilities. It is a common infectious disease, and despite continued publicity is still frequently mistaken for other conditions. Mild fever in a young adult, particularly if he is a student or in some branch of the medical profession, should make one at least suspect the possibility of the disease. Severe headache ushers in most cases and may be mistaken for encephalitis, encephalomyelitis or kindred affections. The spinal fluid in these cases may show lymphocytosis and thus lead to the diagnosis of choriomeningitis or aseptic lymphocytic meningitis. Although the spinal-fluid lymphocytosis is generally regarded as a complication of the disease, it is simply indicative of the widespread lymphoid reaction which may result in perivascular collections of lymphocytes in the brain, and in serous meningitis. Zohman and Silverman⁷ report a case with diffuse lower motor-neurone disease. The throat lesions, although mild in most cases, may be unusually severe in others and accompanied by marked swelling of the neck. If this is so, there is usually a complicating Vincent's infection for which a small dose of neoarsphenamine may be given intravenously. Rarely, the throat reaction may be due to a complicating pneumococcal infection that will respond readily to one of the sulfonamide drugs.

The blood picture shows a well-marked lymphocytosis with the presence of all varieties of lymphocytes, frequently bizarre in shape, size and staining characteristics. The absence of well-defined anemia and of reduction in platelets are two important criteria that should immediately rule out the diagnosis of acute leukemia. However, every rule has its exception. Thus, every so often one sees a case of thrombocytopenic purpura with well-defined lymphocytosis. The diag-

nosis of acute lymphatic leukemia is naturally made, although this can generally be ruled out when the great variability in lymphocytes is noted. In acute leukemia a monotonous blood picture is present, most of the cells being lymphoblasts. As Minot pointed out several years ago, many cases of idiopathic thrombocytopenic purpura present lymphocytosis in which some relatively young forms are rather common. That infectious mononucleosis will occasionally, particularly when splenomegaly is present, result in thrombocytopenic purpura is not well known: I have seen 2 such cases and Brooks⁸ reports another.

A pink macular rash which fades readily on pressure is found occasionally. The mesenteric adenitis with its resultant abdominal pain may result in the diagnosis of acute appendicitis, especially since the leukocyte count is usually elevated. Straus⁹ reports a case in which, although the white-cell count was low, — as it is in about 10 per cent of cases of infectious mononucleosis, — the diagnosis of acute appendicitis was made and operation performed. The appendix was the site of an atypical hyperplasia of the lymphoid tissue, which appeared identical with lesions previously described by Gall in enlarged lymph nodes. It is thus a good rule to consider the diagnosis of infectious mononucleosis in every febrile condition in a youngster or a young adult. Cases in very young children and in people above the age of thirty are unusual. The heterophil agglutination test, using sheep's red cells, is an important diagnostic criterion of the disease. It is positive in about 75 per cent of the cases. Why an antibody is produced that has the specific property of agglutinating sheep's red cells has not been determined, nor has any real advance been made in discovering the infectious agent. A virus etiology has naturally been suggested, and experiments indicating this as a possibility have been recorded by Wising¹⁰ and by van den Berghe and Liessens.¹¹ These investigators introduced glands or blood from patients with the disease into monkeys and produced an infection with suggestive clinical and hematologic features.

Therapeutically, no real progress has been made. As noted above, a complicating Vincent's infection of throat or gums may indicate the use of neoarsphenamine, and sulfathiazole may be used with a complicating coccal organism. I have failed to find any value, however, in the routine use of the sulfonamide drugs, although Hoffman, Lees and Comroe¹² state that sulfathiazole appears to be of definite value in shortening the symptomatic stage of the disease. Lassen and Thomsen¹³ claim benefit from the use of specific convalescent serum in doses of 60 to 300 cc. intravenously. This method probably deserves greater attention in this country

than it has heretofore received, although it must be conceded that most cases are very mild and require only symptomatic treatment. The best thing about the condition is, however, its 100 per cent recovery rate.

In the last few years, a new infection resulting in such phenomena as generalized lymphadenopathy and splenomegaly and caused by the *Histoplasma capsulatum* (Darling) has been described. Wright and Hachtel¹⁴ illustrate a case report of histoplasmosis with some excellent photographs of the organism both in cultures and in tissues. The histoplasmosis is a fungus that has two forms. One is yeastlike and occurs in the blood and reticuloendothelial cells, whereas the other, a mycelial form, develops outside the body in cultures held at room temperature. The yeastlike forms grow only on blood or serum agar at 37°C.

Only about 35 cases have thus far been reported. The symptoms are variable, with irregular fever, lymphadenopathy and splenomegaly outstanding. There may be a moderate normocytic anemia, and leukopenia is usual. As Reid, Scherer, Herbut and Irving¹⁵ point out in a case report, the parasites may be present within the blood cells and recognizable by ordinary blood smears. Sternal puncture in their case showed numerous monocytes and neutrophils containing inclusions resembling superficially Leishman-Donovan bodies. Blood culture is frequently positive, the organism growing out readily after several days either at room or incubator temperature. The disease is very serious and is often but not necessarily fatal. Therapy has not been successful, although antimony has been thought to be of some value.

Miscellaneous

An experimental study which may be of some clinical significance is that of Nettleship,¹⁶ in which heterologous bone-marrow antibodies were produced and injected into the donor animal. An extract of rabbit bone marrow was repeatedly injected into guinea pigs, following which the animals were bled. The guinea-pig serum, presumably containing bone-marrow antibodies, was injected into rabbits. A single large dose produced an indiscriminate necrosis of all the bone-marrow elements, the blood showing leukopenia and anemia. Repeated small doses caused fibrosis of the marrow.

Dameshek and Wolfson¹⁷ direct attention to the possible beneficial effects of the sulfonamide drugs in combating agranulocytosis. Because patients with agranulocytosis do not die of the reduction in granulocytes per se but rather of the resulting secondary sepsis, it was thought that the sulfonamides might be useful in combating the sepsis, the patient's bone marrow meanwhile having an oppor-

tunity to recover. Dramatic recoveries occurred in 2 very severe cases of aminopyrine agranulocytosis in which full doses of sulfathiazole were given. It is worth while remembering that the sulfonamides act by bacteriostasis and may be given with impunity in conditions with marked leukopenia.

With respect to the bone marrow, sternal puncture as a diagnostic help becomes ever more popular. As Mendell, Meranze and Meranze¹⁸ report, it is virtually diagnostic in acute leukemia, aleukemic leukemia, multiple myeloma, leishmaniasis, malaria and Gaucher's disease. I believe that when taken in conjunction with the blood picture the bone-marrow biopsy is all important in the study of cases of obscure or refractory anemia, and in anemias accompanied with increased hemolysis. Simple puncture is usually satisfactory, and in any event can always be done as a preliminary method. It is only occasionally necessary to resort to trephine biopsy of the sternum, a measure that becomes of value in assessing the general architecture of the marrow tissues, as in aplasia, fibrosis or certain cases with neoplastic infiltration. Shapiro and Bassen¹⁹ report their methods and the results obtained in studying the sternal marrow during the first week of life. They found that the formation of the red cells becomes suddenly curtailed during this period, perhaps because of the better oxygenation present in the outside world.

The blood volume in normal infants and children has been studied by Brines, Gibson and Kunkel,²⁰ using the dye Evans blue and a photoelectric colorimeter. The total volume, about 300 cc. at birth, doubles during the first year of life, and thereafter increases until puberty, when it is about 2500 cc. Both plasma and total volume are more closely related to physical size than to age, and may thus be predicted on the basis of the child's height, weight or surface area to a degree of accuracy sufficient for practical purposes. Some interesting studies on the response of normal subjects to acute blood loss have been made by Ebert, Stead and Gibson.²¹ The blood loss was observed under controlled conditions in 6 subjects from whom 760 to 1220 cc. of blood was withdrawn. The decrease in blood volume by hemorrhage was compensated in two ways: by vasoconstriction and by the addition of fluid to the blood stream. The change in hematocrit percentage accurately reflected the direction of the changes in the plasma volume in these experiments. Thus the continued increase in plasma volume was not well shown by a decrease in protein concentration but by a steady fall in the hematocrit reading, since the red-cell volumes remained relatively constant during a period of three days. These findings are important from the standpoint of studying cases of severe

blood loss with or without accompanying shock. The production, utilization and interrelation of hemoglobin and plasma proteins are discussed by Whipple²² in a review of the fundamental work which has been carried on for years in the famous dog colony and laboratories of the University of Rochester Medical School.

BLOOD TRANSFUSIONS AND BLOOD GROUPS

Owing of course to the exigencies of war, the transfusion of blood and plasma has assumed tremendous importance. By now everyone is familiar with the life-saving qualities of plasma in traumatic, hemorrhagic and surgical shock. Plasma, replacing as it does the fluid lost from the circulating blood, is an urgent necessity. Numerous methods have been published for preparing, storing, freezing, drying and administering plasma. In a series of articles, Strumia, McGraw and Reichel^{23, 24} give detailed directions for its preparation and preservation. These writers strongly advocate centrifugation of the blood to increase the plasma yield, and storage of the plasma in a frozen state. They claim that the latter procedure reduces infection to a minimum, and that this possibility may be still further reduced by collecting the plasma from the whole blood within twenty-four to forty-eight hours after its removal. In their fourth paper, the preparation of dried plasma is considered. The latter is of special value because it permits safe and prolonged storage and transportation under adverse conditions, and because the plasma may be reconstituted in a concentrated form for such conditions as edema of the brain. The methods developed by Strumia et al. have been widely utilized.

At the Army and Navy Blood Plasma Division in Washington, headed by Commander Newhouser^{*} of the Navy and Lieutenant Colonel Kendrick of the Army, plasma is stored in liquid form (with added Merthiolate) or kept frozen. Both the liquid and the frozen plasma are shipped throughout the country for use at various Army and Navy posts. Dry plasma, which is prepared by pharmaceutical houses from part of the donated blood, is used only for shipment abroad. Both liquid and frozen plasma have been found eminently satisfactory. Liquid plasma prepared by a *closed method with scrupulously aseptic technic* has been stored for at least twelve months at room temperature. When thus carefully handled, it not only remains free from bacterial contamination but is satisfactory for immediate use in shock. Furthermore, it does not require melting from the

frozen state nor reconstituting from the dried product.

Novak²⁵ recommends the use of one of the sulfonamides, preferably sodium sulfathiazole, in the preservation of blood plasma in a liquid state. A solution of 1.5 gm. of sodium citrate and 1 gm. of sodium sulfathiazole in 50 cc. of normal saline is used for 450 cc. of blood, giving a concentration of sulfonamide of 0.2 per cent. This method has been criticized by some and is not generally accepted.

Crosbie and Scarborough²⁶ present a series of studies on stored blood, which deal with such matters as the fate of the red cells, leukocytes and platelets, together with prothrombin content, coagulation time and so forth. These factors are also considered by Strumia and McGraw.²⁷ It is apparent that the drying of plasma results in the loss of almost all the prothrombin and of a portion of the complement present in liquid plasma. Since complement may be of value in combating infection, the use of dried plasma alone, as in burn cases, may not be completely desirable.

Work on the preparation of albumin from human and bovine blood has been vigorously pursued. From the standpoint of osmotic pressure and the retention of fluids within the vascular tree, albumin is of far greater importance than serum globulin. Thus, Newhouser and Lozner²⁸ have reported that 25 gm. of human albumin is osmotically equivalent to 500 cc. of citrated plasma, provided the patient is normally hydrated. It may be given in a small volume (100 cc.) of solution, and has a greater plasma diluting effect than twice the ordinary 250-cc. unit of plasma. This material, one of the chief advantages of which is its small bulk, is now being packaged for use in the Navy. It is chiefly of value as an emergency first-aid measure and its use has thus far been circumscribed by numerous precautions. At present, it cannot replace whole plasma.

A community method for the collection, preservation and distribution of plasma has been described by Gottlieb and Clapperton.²⁹ The existing fourteen community hospitals centering about the Central Maine General Hospital at Lewiston are utilized. All the bottles, apparatus and so on are prepared at the central hospital. In the community hospitals, blood is drawn from volunteer donors and is shipped to the central hospital, where it is processed. Part of the plasma is left in a large refrigeration unit at Lewiston, the remainder being returned to the community hospitals. In the event of disaster, the stock of plasma at the central station can be made immediately available for any of the smaller hospitals.

*I am indebted to Commander L. R. Newhouser (MC), U.S.N., for his kindness in verifying the statements relating to the Navy work with blood plasma and albumin.

All the bottles, apparatus and so on are prepared at the central hospital.

The question of the rate of hemoglobin regeneration in blood donors has been studied by Fowler and Barer³⁰ who found that the average time required to replace 550 cc. of blood was 49.6 days. Some subjects, on the other hand, required three months. With iron therapy, the average recovery time was shortened to 35.2 days. Fowler and Barer suggest that unless hemoglobin levels are regularly determined, an interval of three months between blood donations should be allowed.

The infusion of blood and other fluids into the bone marrow has assumed some importance, since the sternal-marrow space is almost always readily available, at least in adults and older children, whereas veins may at times be inaccessible. Tocantins and his co-workers¹¹ have demonstrated that substances injected into the bone-marrow cavity are immediately taken up into the venous circulation. The method is particularly applicable in infants and in patients with collapsed veins, as in shock, and when veins are completely inaccessible, as in patients with extensive burns. In infancy, below the age of two, the needle is introduced into either the upper end of the tibia or the lower end of the femur. Fluids, including blood, are introduced either by gravity, or by positive pressure if more speed is desired. For further details of the techniques involved, the original papers should be consulted. Tocantins has recommended a special double needle. By the use of a simple sternal-puncture needle,* however, Doud and Tysell³² administered 9025 cc. of whole citrated blood and 13,950 cc. of fluids to a patient with uncontrollable hemorrhage from the bowel due to ulcerative colitis. The needle remained *in situ* for several days at a time without evidence of infection or other complication. When blood or fluids were not being administered, the needle stylet was replaced. In this case, the procedure seemed definitely lifesaving.

There is some controversy regarding the use of so called "universal donors" (Group O). Although most authorities now believe that the blood of these donors, because of its content of anti-A and anti-B agglutinins, is inadvisable for use in Group A, B and AB recipients, this is contradicted by others, for example Rosenthal and Vogel.³³ An analysis by these investigators of 819 transfusions with universal donors has shown that such transfusions are not followed by any greater number of reactions than are those with homologous blood. They believe that the universal donor is both reliable and safe for citrate transfusions in emergen-

cies, either in civil practice or in the armed forces. My own experience indicates that in severe anemia, and particularly in hemolytic anemia, it is unwise to use anything but homologous donors. The agglutinin content of the universal donor's blood plasma, although safe enough in ordinary cases, may be high relative to the cells of severely anemic blood, more particularly when spherocytosis is present. Furthermore, in hemolytic cases the possibility of an isohemolysin or atypical intragroup agglutinin is always present.

Hemolytic reactions following transfusions of blood of the homologous group, with particular reference to the Rh factor, are described by Wiener.¹¹ It is possible to immunize an individual of the same blood group but who is Rh- with Rh+ blood, with the result that he develops an anti Rh agglutinin. When another transfusion of Rh+ blood is then given, agglutination of red cells takes place within the patient's circulation, with a resultant hemolytic reaction. Wiener advocates that whenever possible, homologous Rh blood be used in repeated transfusions. A safe universal donor, according to this author, is one of Group O, Rh-, with a low titer of isoagglutinins in his serum. To guard against the possibility of an atypical hemolysin or agglutinin, it is necessary to perform careful compatibility tests when repeated transfusions are given. These are done by the Landsteiner-Levine test-tube technique, in which 1 drop of 2 per cent red-cell suspension, 1 drop of serum and 1 drop of saline are incubated at 37° C. for half an hour, following which the mixture is examined both macroscopically and microscopically for agglutination. An ingenious method of utilizing Group O blood for universal-donor transfusions is the addition to the drawn blood of A and B substances, as developed by Witebsky and his co-workers. These substances, carbohydrate-like in nature, possess the properties of the A and B agglutinogens and therefore absorb or neutralize anti-A and anti-B agglutinins normally present in Group O plasma. A solution containing the A and B substances is being prepared by a pharmaceutical house for clinical use. Further investigations by Witebsky and Klendshoj³⁵ have resulted in the isolation of an O specific substance from gastric juice. This gives additional evidence of the presence of an O agglutinin, although usually the dictum has been that no such substance is present, and that Group O cells are devoid of both A and B substances.

PERNICIOUS ANEMIA AND RELATED STATES

Pathogenetic Mechanisms

The vexing problem regarding the site of origin of Castle's intrinsic factor has been investigated in

*Manufactured by the Becton-Dickinson Company, Rutherford, New Jersey, or the Hub Needle Company, Boston

the pig by Meulengracht and more recently in the human being by Fox and Castle.³⁶ Meulengracht assumed that of the various available animals for study the stomach most closely comparable to the human one was that of the pig. He found that in this animal the region of the pylorus (pyloric gland organ) was hematopoietically active, whereas the fundic portion was inactive. In human pernicious anemia, on the other hand, it is the fundic glands that are regularly involved, the pyloric portion remaining histologically normal. Meulengracht then formed the rather striking hypothesis that the fundus acts simply as an initiator or pacemaker of the pyloric-gland region, and that in the absence of this initiator there is no secretion of intrinsic factor. However, as Fox and Castle point out, these pieces of evidence become contradictory "only when conclusions which undoubtedly obtain for the hog are directly translated to man." These investigators demonstrated that extracts made from human stomachs showed very little if any activity in the pyloric region, although marked activity in the fundic regions was present. Thus there is a direct correspondence of the histologic lesions of the stomach of pernicious anemia with the physiologic experiments carried out with human material.

The neurologic lesions of pernicious anemia are often out of all proportion to the extent of the anemia. Conversely, many classic cases with outspoken anemia have minimal neurologic disturbances. This dissociation between the hematologic and neurologic changes has led many investigators to speculate that they may be due to different types of deficiency. Wintrobe and his co-workers have for many years tried unsuccessfully to reproduce in animals the hematologic changes of pernicious anemia. However, in the course of their investigations, the neurologic manifestations have been faithfully reproduced by the use of a diet deficient in various fractions of the B complex, but in which thiamin, riboflavin and nicotinic acid were supplied.³⁷ Wintrobe's investigations have cast doubt on thiamin as the anti-neuritic vitamin. In these studies, the neurologic lesions were completely prevented by the use of potent liver-extract preparations given orally and by the use of pyridoxin (B₆), pantothenic acid and perhaps choline. Is the deficiency of these substances then the cause of the neurologic lesions of pernicious anemia? This question and the problem of the exact relation of these studies in swine to human disease remain to be answered. The continued failure of many different groups of investigators to reproduce in animals the typical hematologic disturbances of pernicious anemia suggests either that a deficiency state may produce results in man different from those in experimental animals, or that the concept of the intrinsic factor, its forma-

tion, elaboration and so forth is only partially explanatory of the pathogenesis of the disease.

Certain cases of pregnancy are associated with the typical blood changes of pernicious anemia. The gastric analysis may show free hydrochloric acid, and complete recovery may occur after a period of liver-extract therapy. Segerdahl³⁸ studied the sternal marrow of several cases and found megaloblastic and leukocytic changes as seen in typical pernicious anemia. There can thus be no doubt that a liver-extract deficiency accounts for the development of these cases. Whether this is dietary in origin or due to a large abstraction of material from the mother by the fetus is not clear. Liver extract alone is often only very slowly curative, and transfusions are also required in a few cases.

Not all macrocytic anemia is pernicious anemia. Thus, the macrocytic anemia of hepatic disease, more particularly cirrhosis, does not necessarily indicate that there is a deficiency of the liver-extract principle. In the experience of practically all investigators, purified liver extract produces little if any change in the blood picture. Furthermore, the demonstration by Schiff and his co-workers³⁹ some years ago that the specific antianemic substance is present in human livers with cirrhosis indicates that the two macrocytic anemias are of entirely different origins. Rarely, pernicious anemia with the typical bone-marrow findings and response to liver extract is coexistent with cirrhosis. Ratnoff and Patek⁴⁰ found 2 such patients in their series of 386 well-studied cases.

The blood picture of sprue, both tropical and nontropical, differs in several small respects from that of Addisonian pernicious anemia. The red cells are regularly macrocytic without much change in size or shape, the platelets may be normal, the bilirubin content of the blood is usually low, and so on. Furthermore, free hydrochloric acid is present in the gastric juice of most patients; the bone marrow is hardly megaloblastic in character; there are severe intestinal disturbances, often associated with hypocalcemia; the sugar-tolerance curve is flat; and the response to liver extract is either sluggish or nil.

Hanes⁴¹ describes several cases of the sprue syndrome (including celiac disease and sprue), and Molina⁴² describes 100 cases of tropical sprue. Extreme muscular wasting was striking in Molina's cases. Direct examination of the gastric and rectal mucosa showed changes similar to those seen in the tongue and pointed to faulty absorption of food products by the bowel. Although a deficiency state is undeniable, the fundamental cause of the intestinal malabsorption is still obscure. The concept advanced by Castle and Rhoads in 1935 that a deficiency state similar to if

not identical with pernicious anemia is present is questioned by Molina, who points to the severe intestinal dysfunction as the most prominent feature of the disease. This may be due to the continued use of fried or greasy food and of cereals, with resultant irritability of the bowel. The x-ray findings in the small intestine in sprue and in vitamin B deficiency are beautifully described by Golden.⁴³ A deficiency pattern, centering about changes in the small bowel, is pictured in which the prominent features are hypermotility and later hypomotility, abnormal segmentation, "scattering effect," gas and fluid levels, changes in the mucosal membrane and so forth. These changes frequently respond strikingly to liver-extract or yeast therapy. Further studies along the same lines are presented by Lepore and Golden.⁴⁴

Treatment

A number of experimental studies have recently appeared dealing with further attempts at using the experimental animal for the assay of liver-extract preparations. Several of these studies have dealt with the supposedly megaloblastic, liver-extract-deficient type of hematopoiesis in the embryo. Thus, Stasney and Higgins several years ago used the newborn rat, and more recently Stasney and Burns⁴⁵ utilized young opossums, which are conveniently situated (like kangaroo young) in a pouch and yet are embryonic. The changes in the size of the red cells after administration of liver extract has been utilized by these observers as a criterion of response to therapy. Jones⁴⁶ used pregnant rats from which eleven-day embryos were obtained. Blood smears of the yolk sac of the embryo were stained and the red-cell and nuclear diameters were counted both in control animals and in those in which the mothers had been given either gastric or liver-extract preparations. The assumption was of course made that the erythrocyte-maturing principle had passed across the placental membrane. Jones demonstrated a definite effect on erythropoiesis in the embryo as indicated by a reduction in the mean cell and nuclear diameters of the primitive erythroblasts. Ventriculin concentrate was most effective. The results of both Stasney and his collaborators and of Jones have been questioned by Last and Hays,⁴⁷ who found that statistical analysis of the data indicated that the responses in the treated animals were within the range of biologic variation. They concluded that neither opossum nor rat embryos should be used in the bioassay of antianemia preparations. The mildly polemic postscripts of Jones *vs.* Last and *vice versa* make interesting reading. Further studies by Hays, Last and Koch⁴⁸ indicate that erythropoiesis in the three-to-seven-day-old chick embryo also cannot be utilized for assay purposes.

For the present, one must still be content with human assay material, which is, however, scarce and often difficult to control.

The striking changes in the bone marrow from a megaloblastic picture to one that is normal (normoblastic) in type are further discussed by Davidson, Davis and Innes.⁴⁹ Dameshek and Valentine⁵⁰ several years ago investigated the changes that occur and interpreted them as a change from a liver-extract-deficient megaloblastic erythropoiesis to a liver-extract-satisfied normoblastic type. Davidson et al. claim that the megaloblast is not specific for liver-extract deficiency and interpret the rapid changes after treatment as indicative of a normal type of erythropoiesis. My own interpretation of the same phenomena, which is radically different, seems borne out by bone-marrow studies in various other deficiency syndromes.

The clinical use of liver-extract therapy is considered in a group of articles by Evans and Jordan,⁵¹ Strauss, Patek, Pohle, Fox and Burchenal,⁵² and Seymour, Heinle and Miller.⁵³ Evans and Jordan found that a highly concentrated liver-extract preparation (Reticulogen) was far more effective than less concentrated extracts, not only in controlling the blood counts but in improving the neurologic lesions. Strauss and his co-workers, after an initial bias for the very crude extracts, have now adopted a uniform maintenance dose of 15 U.S.P. units of purified liver extract every four weeks. During eighteen months of this regimen no subjective or objective relapses in the blood, gastrointestinal or nervous system were observed. Seymour et al. found that patients differed in their ability to store large quantities of liver extract given in relapse. This difference probably depends to great extent on the degree of intrinsic factor lack and to some extent on the diet (that is, the potency of the extrinsic factor).

(To be concluded)

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**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL**

ANTE MORTEM AND POST MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, MD, *Editor*

CASE 29051

A seventy five year old woman was referred to this hospital because of difficulty in swallowing, epigastric discomfort and nervousness.

Twenty five years before entry, the patient felt a nodule about the size of a walnut on the left side of the neck. Her physician said that her basal metabolic rate was normal and that the nodule had no significance. Thirteen years later, because of a "nervous spell" characterized by headaches, nervousness and mental uneasiness, she consulted a local clinic. At that time there was no sweating, palpitation, tremor or diarrhea and the neck nodule had not increased in size. At this clinic, because of an apparently normal x ray film of the chest and an unremarkable basal metabolic rate, the patient was told that the neck nodule would never bother her. Five months before entry she noticed that food seemed to stick in her throat, and several days later her neck began to swell. Six weeks before entry, her physician advised an operation on the "goiter," and four weeks later she entered a community hospital. There an x ray film of the upper chest and neck revealed an "adenomatous goiter" that extended 4 to 5 cm below the clavicles, the trachea was deviated to the right. The blood cholesterol was 215 mg per 100 cc, and the basal metabolic rate was -10 per cent. She was treated with a course of x ray radiation to the neck in five divided doses, following which her neck became swollen. She was referred to this hospital for further care. She had never noticed exophthalmos, palpitation, sweating, tremor, diarrhea, jaundice, abdominal pain or tarry, bloody or choleric stools.

The family and past histories were noncontributory.

Physical examination revealed a dyspneic and orthopneic woman who did not appear to be in great distress. The left pupil was larger than the right, but both were round and reacted to light and accommodation. The thyroid gland was enlarged on both sides, particularly on the left, and extended beneath the sternum; it seemed quite firm, but no discrete nodules were felt and no bruit was audible. The external jugular veins

were prominent over it, and the trachea was deviated to the right. The heart was not enlarged, and the sounds were of good quality, occasional extrasystoles occurred, but no murmurs were audible. The examination of the lungs and abdomen was negative. There was fixation of the left vocal cord, and some compression of the infraglottic airway.

The blood pressure was 170 systolic, 90 diastolic. The temperature was 97°F, the pulse 89, and the respirations 24.

Examination of the blood revealed a hemoglobin of 80 per cent and a white cell count of 7700. The urine was acid in reaction and gave a "green" sugar test and a + test for albumin, the sediment contained 15 to 20 white cells and 1 or 2 red cells per high power field. The sugar test was "blue" on two subsequent examinations.

An x ray film of the chest, including the neck, demonstrated a large soft tissue mass occupying the position of the thyroid gland, measuring 10.5 cm across and extending subcutaneously to the level of the aortic arch. The mass was of considerable density. The chest was narrowed laterally. The diaphragm was low in position and showed limited motion on both sides. The lung fields were unusually bright, and there was an increase in the markings. The heart was small. An electrocardiogram demonstrated a normal sinus rhythm of 90. The PR interval was 0.14 second, the T wave was isoelectric in Leads 1, 2 and 3, and T₄ was shallow, the ST segment in Leads 2 and 3 was slightly depressed.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR SAUL HERTZ: I should like to emphasize that the patient found the nodule and went to her physician. I think the lump that the patient finds is probably more significant than the one that the doctor finds. For a patient to remember twenty five years back is an important point in the diagnostic elements of the case. The physical examination later describes a uniform enlargement in the region of the thyroid gland and that is why I am making this point about the patient's description of the nodule. Apparently the physicians in the clinic that the patient visited found the same thing and confirmed the patient's finding.

We are not certain whether it was truly the thyroid gland that was involved. The fact that she was treated with x ray radiation seems to indicate that her physicians were thinking of lymphoma, and gave a therapeutic x ray trial, apparently without a biopsy. The swelling after x ray therapy might point to some form of lymphoma,

but I do not believe that is a significant point in the differential diagnosis; however, the lack of response is.

We are left, then, with an old lady with a twenty-five-year-old mass in her neck, which apparently had undergone certain changes in the previous twelve years, particularly in the previous five or six months. On physical examination, dyspnea and orthopnea were found in a person who was described, nevertheless, as not being in great distress. Orthopnea may not be distressing for some people, but I am sure it would be for me. One would like to know whether they thought the orthopnea was associated with definite stridor. That would be important in ascertaining the degree of compression of the trachea and would help quite a bit.

The dilatation of the pupil on the left indicates stimulation of the cervical sympathetic nerves on that side. It seems to indicate disorder in the left lobe of the thyroid gland, if it was the thyroid gland, compressing the recurrent laryngeal nerve and causing paralysis of it. We are told later that the vocal cord on that side did not move.

The description of the gland is of value in trying to diagnose this case. I should like to be sure that it was uniformly enlarged and non-nodular, because it makes all the difference in the world in defining this case as cancer of the thyroid or chronic thyroiditis. A picture similar to this can be produced by the invasive type of chronic thyroiditis, Riedel's struma, causing involvement of the recurrent laryngeal and sympathetic nerves. Apparently there was also some interference with venous circulation, pointing to an upper mediastinal syndrome, conceivably on a lymphomatous basis.

The deviation of the trachea to the right is significant because it tends to indicate that the disease was well defined on the left and possibly that the old nodule had something to do with the recent disorder. In the past history of cases of thyroid cancer, the finding of pre-existing goiter is frequent.

The invasive character of the mass in the neck is in favor of either carcinoma or chronic thyroiditis; although a nontoxic goiter that has expanded because of hemorrhage or cystic degeneration may cause considerable pressure on the recurrent laryngeal nerve and give a picture similar to this, I think it unlikely.

At the age of seventy-five, with a nodule of many years' duration, which I am taking seriously, carcinoma has to be considered as the first possibility. However, the fact that the thyroid gland is described as uniform makes me lean toward chronic thyroiditis. I think the x-ray film will be helpful and should like to see it at this point.

DR. LAURENCE L. ROBBINS: This is the mass that lies in the region of the thyroid gland. It is practically symmetrical on both sides, and extends down to the level of the aortic arch. I notice that the report said that the mass was of considerable density. They probably meant ordinary soft-tissue density. I do not believe that there are areas of calcification within the mass; there is a fleck here but it is probably pleural or in the lung. The remainder of the chest shows considerable emphysema and questionable early fibrosis.

DR. HERTZ: The x-ray film suggests that the mass was uniform. I cannot remember having seen a case of chronic thyroiditis in which the mass extended into the thorax to this extent, and I tend to rule it out on that basis. That brings me down to one diagnosis—thyroid carcinoma in a long-existing nodular goiter. There are a few rare conditions that should be considered. Could this be something other than the thyroid gland, even though the x-ray man and the clinical examiners indicated that the thyroid gland was involved, and the early story centers around the thyroid nodule? Perhaps the unusual turned up here, and I should like to put on record the possibility of carcinoma of the esophagus or bronchus, since the patient complained of dyspnea. But I doubt whether these would cause metastasis to the mediastinum of this type without more characteristic glandular metastasis in the neck. If this was an extrathyroid cancer it manifested itself in an odd way. There is also a bare but unlikely possibility that this was a benign tumor, a nontoxic nodular goiter.

CLINICAL DIAGNOSES

Tracheal obstruction, due to colloid goiter.
Arteriosclerotic heart disease.

DR. HERTZ'S DIAGNOSIS

Carcinoma of thyroid.

ANATOMICAL DIAGNOSES

Malignant lymphoma, stem-cell type, of cervical and mediastinal nodes.
Nodular colloid goiter.
Tracheotomy.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Shortly after entering the hospital the patient developed symptoms of marked respiratory obstruction; it was believed that emergency relief was required so a tracheotomy was done and a small portion of the mass was removed, in part as a biopsy and in part with the hope of relieving some of the tracheal obstruction. Microscopic examination showed a benign colloid goiter. Following the operation, the patient ex-

perienched little relief and had successive episodes of severe tracheal obstruction, some of which could be relieved by aspiration of the tracheal secretions; she eventually died with respiratory obstruction.

The autopsy showed a large tumor mass in the upper mediastinum and lower neck that completely encircled the thyroid gland but did not involve it. This turned out to be a malignant lymphoma of the undifferentiated or stem-cell type. The thyroid gland was only slightly enlarged, and we did not find any particular area that we were convinced was the mass the patient had noted for twenty-five years. That must have been lost in the general tumor mass.

DR. HERTZ: I want to emphasize one point. We are often asked what to do about a single nodular goiter. Frequently the history is given that the patient has had such a mass for twenty or more years. Here is a case in point. How much can we trust the history in dealing with nontoxic nodular goiter? It is of no great diagnostic value to us unless we have seen the nodule ourselves and have made up our minds that it did lie within the thyroid gland. But nothing is said in the record whether the mass rose and fell after deglutition, an observation that should be recorded in any description of a case where the possibility of thyroid disease is considered.

DR. MALLORY: I think that all the examiners felt quite sure that it was thyroid gland, including the surgeon who operated on her, who still thought the obstruction was due to the goiter when the operation was over.

CASE 29052

PRESENTATION OF CASE

A fifty-nine-year-old widowed housekeeper entered the hospital because of a vague epigastric distress that often interfered with her sleep.

During most of her adult life the patient had, like her mother before her, suffered with brief attacks of "biliousness" that occurred once or twice each year and spontaneously disappeared. Occasionally during these episodes she vomited small amounts of green, bitter fluid and had shaking chills. Four months before entry vague epigastric distress developed and often interfered with her sleep. The discomfort bore only a questionable relation to meals and was not relieved by soda. At no time did the vomitus contain blood or coffee grounds, and she never had diarrhea, constipation, jaundice, melena or weight loss. Nine days before admission a physician felt an egg-sized lump in the abdomen and advised hospitalization.

The family history was noncontributory. The menopause had occurred seven years before entry,

and the uterus was removed because of fibroids three years later.

Physical examination revealed a sallow, middle-aged woman in no distress. The examination of the heart was negative. A few crackling rales that did not disappear on coughing were audible at the base of the right lung. In the upper midepigastrium just below the xiphoid there was an egg-sized, firm, rounded, slightly tender mass that was quite movable, descended only slightly with respirations and seemed to pulsate.

The temperature was 98.9°F., the pulse 81, and the respirations 19.

The urine was negative. The blood Hinton was negative. A barium meal revealed a normal esophagus. There was a pressure defect on the lesser curvature of the stomach in the region of the angle; this was due to extrinsic pressure, and there was no evidence of intrinsic disease. The duodenal loop was not remarkable. At the end of six hours the barium lay on the proximal colon.

On the fourth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ERNEST DALAND: This patient's symptoms really date back four months although there were indefinite symptoms before that. She had had no vomiting of blood or coffee-grounds material, suggesting that her difficulties had no intrinsic relation with the stomach. There was no diarrhea, constipation or jaundice, which is important. She had had a hysterectomy four years before entry. It is presumable that the operator passed his hand around the epigastrium at the time of operation and that this mass was not there at that time. An egg-sized, firm, round, slightly tender mass was felt at this admission. Those of you who have operated on an extensive cancer of the stomach that has not been felt beforehand must have been impressed with the size of a tumor that can be hidden in the epigastrium without being palpable. Here we have an egg-sized mass that the local physician felt, and also the man on the ward.

The first thing one would have to think of is an epigastric hernia. There is no note whether there was any impulse on cough, but many times in an epigastric hernia there is no impulse. However, as we go on and find that the x-ray films showed a pressure defect on the stomach I think we can rule out anything in the abdominal wall. There was something within the abdomen.

I should like to see the x-ray films. The number of structures that we have to consider in this region are distinctly limited. The left lobe of the liver may sometimes be palpated but would not be picked up as an egg-sized mass. The pancreas is

located here, as well as the stomach wall, the lymph nodes along the lesser curvature and the aorta. These are the organs that we have to consider.

DR. MILFORD D. SCHULZ: This I believe is the defect caused by the extrinsic mass that was described. You can see that the rugal folds pass uninterrupted over the area. The same is true in this spot film, which confirms the opinion of the fluoroscopist that this was an extrinsic mass. I think we might note that there is no evidence of erosion of the vertebrae so far as can be seen on these films.

DR. DALAND: Might it be something in the stomach wall and still have the rugae normal without ulceration?

DR. SCHULZ: Yes; but you would expect to see some displacement of the folds as they pass over the mass in the stomach wall. If it is intramural, there is usually some point of ulceration.

DR. TRACY B. MALLORY: However, myomas can be pedunculated and hang externally and not necessarily show any thickening of the stomach wall.

DR. SCHULZ: Yes; but then it often shows some evidence of tug on the stomach.

DR. DALAND: First is the question of aneurysm. The mass was said to be pulsating. There is no note whether there was any bruit on stethoscopic examination, or whether there was any expansile pulsation. There are no lateral films. A lateral film would probably have been taken if they had a strong suspicion of aneurysm, since it might have demonstrated erosions of the vertebrae that could not have been seen in the anteroposterior view. I think we can discount the possibility of aneurysm. In this plain film there is a shadow. Is it a mass?

DR. SCHULZ: It is rather indefinite.

DR. DALAND: I was given permission to look at these films before the conference and that was the only suspicious thing that I saw.

DR. SCHULZ: Of course, it could be a mass.

DR. DALAND: The pancreas is the next thing to be considered—a cyst of the pancreas or a tumor of the pancreas. Ordinarily, pancreatic cysts are in the loop of the duodenum—that is, if they arise in the head of the pancreas. However, the pancreas does extend across the midline at about this point and it would be possible for a cyst of the pancreas to present here; a lateral view would help a good deal in deciding whether the stomach was pushed forward. I thought tumor of the stom-

ach wall was a definite possibility; a benign leiomyoma of the stomach wall which had been there for some time might produce this picture. A malignant leiomyosarcoma would probably have ulcerated by this time and would give a defect on the inside of the stomach. The commonest tumor of the stomach next to carcinoma is leiomyoma, and I think that that is a decided possibility.

The other possibility is lymphoma. Such a tumor may occur in any place where there are lymph nodes, and this is a suitable location. There is no evidence of lymphoma anywhere else, and since the difficulty had apparently been going on for four months, I think that if it had been lymphoma there would have been other evidence of the disease.

I believe that this was a cyst of the body of the pancreas.

DR. FRED A. SIMMONS: I assisted at the operation on this patient. The house officer was given his choice of diagnoses after having had the privilege of palpating the abdomen under anesthesia; he chose pancreatic cyst. I was given a choice and chose leiomyoma of the stomach. The surgeon with his mature judgment said hydrops of the gall bladder. The mass was definitely to the left of the midline and larger than an egg, being 10 cm. long and 5 cm. broad. It was hard, movable and not adherent.

CLINICAL DIAGNOSIS

Hydrops of the gall bladder?

DR. DALAND'S DIAGNOSIS

Cyst of body of pancreas.

ANATOMICAL DIAGNOSIS

Hydrops of gall bladder.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was explored and an enormous gall bladder was found, which crossed anterior to and above the stomach, producing a pressure defect on the lesser curvature. When finally explored, it turned out to be even bigger than it seemed under anesthesia. It was 15 cm. in length and nearly 10 cm. in diameter, and it contained clear mucinous fluid and a considerable number of stones. I also called it a pancreatic cyst when I read the record, Dr. Daland. A lateral x-ray examination would probably have told the story.

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THE LABORATORY IN WARTIME

Now that medical personnel has been heavily depleted for the needs of the armed services, it becomes increasingly important that the practitioners still caring for the civilian population be able to carry on the work they do with the highest degree of efficiency.

An important factor in diagnosis and in the control of treatment is the information made available by the laboratory. The aid that a positive serologic reaction for syphilis may give in unraveling a diagnostic puzzle is as striking as the information that roentgenologic examination gives to the surgeon in a case of fracture or that hematologic studies afford to the internist studying a case of pernicious anemia or leukemia. Hardly the surgeon who trusts to his gross examination

of a removed lesion to determine whether malignancy is present.

One of the striking developments in medicine of the past two decades has been the phenomenal expansion of the use of the laboratory. Laboratory procedures have opened up new investigative techniques and have done much to simplify the understanding of many pathologic processes. So much can be done by the laboratory that it has sometimes received an unfair share of the diagnostic burden. Fifteen years ago the determinations of blood sugar levels, of sedimentation rates and of the amounts of serum protein were more or less rarities; but today, fortunately, they are matters of everyday performance and a requisition slip sent to the laboratory elicits prompt information concerning the desired test.

These laboratory procedures have different degrees of usefulness, and the complexity and reliability of the tests also vary to an appreciable degree. Such tests as the number of white cells, the amount of hemoglobin and the level of non-protein nitrogen in the blood may be carried out with great accuracy and dispatch. On the other hand, methods such as the hippuric acid test for liver function and the test for serum amylase may be neither accurate or informative.

Although it is easy in most hospitals to requisition any amount of laboratory work, all too often these studies are demanded without regard to the clinical condition of the patient and without any clear idea of what positive information may be obtained and what are the limitations of the tests. Much laboratory work that is useful under a certain set of circumstances is valueless or of academic interest under others, and it is worth while for the physician to check over his written orders from time to time to make sure that he really gets significant and useful information from the laboratory. Thus, several years ago pneumococcal typing was of great importance as an emergency procedure. Now, with the widespread use of the sulfonamides typing is unnecessary except in those cases in which serum therapy is also used.

Laboratories have suffered by the loss of pathologists and by the loss of technicians, and a curtailment of the scope of their work is inevitable. If their important help is to be utilized to best advantage, it is essential that there be discrimination by the practitioner in the laboratory tests that he requisitions. Thus, the performance of a complete blood count is undoubtedly of some interest in every patient seen. Unless there is some clinical indication to the contrary, however, a hemoglobin determination is all that is actually necessary, and if it proves abnormal, this serves as a starting point for further investigation. Similarly, a serologic test for syphilis is desirable for every patient, but there is rarely need for this request to be accompanied by one for gonococcal complement fixation and typhoid, paratyphoid and undulant fever agglutination.

Another waste in laboratories is the performance of scattered tests at frequent intervals. Many tests are not of an emergency nature. It is most conserving of laboratory personnel and material if several such tests can be done at the same time, even though it entails two or three days' delay. In this group fall such tests as the determination of blood calcium and phosphorus, of blood cholesterol, and of serum phosphatase.

It also behooves each pathologist to check over the work done in his laboratory, to make sure that there are no ways overlooked in which the available material and personnel can be used to better advantage. Even the tissue pathologist might well consider whether the lengthy microscopic descriptions that take his time to dictate, the secretary's time to typewrite and the surgeon's time to read are really worth the effort and give enough additional information to justify their retention in place of the microscopic diagnosis alone.

All too often in these days it is difficult to get adequate laboratory work done for the patient outside the hospital, and it is almost impossible for the physician to have a technician in his own office. Fortunately, several private laboratories and some hospital laboratories are available for the carrying out of essential labora-

tory tests for such patients. It might be well worth while for all hospital administrators to consider making available the laboratory facilities of their hospitals, so far as it is possible without impairing efficiency, to those practitioners who find themselves in need of data the laboratory can supply.

SAFE DELIVERANCE

A NEW book by a Boston physician, Dr. Frederick C. Irving,* deserves special attention.

The text is divided into three sections. The first is an autobiography of the author, written in an engaging style. There is much of interest in the account of his early life, particularly regarding his grandfather, a physician who practiced in northern New York, served through the worst battles of the Civil War and passed on his enthusiasm for medicine to his grandchild. Dr. Irving has paid a fine tribute to a man of character and *makes one realize that many of the best things in medicine are not entirely due to the great advances in recent years—character in a physician is still a primary and necessary asset.* Then come reminiscences of life in Harvard College at the turn of the century and of teaching at Harvard Medical School. The chapters on experiences at the Boston Lying-in Hospital on McLean Street are of great interest, and no one except the inimitable "Fritz" Irving could tell the story as he has done it. There are descriptions, too, of his period as a house pupil at the Massachusetts General Hospital, of which those dealing with the life in the hospital itself and with sidelights on Maurice Richardson and other surgeons are of particular interest. After a brief interval of war service, Dr. Irving returned to this country in 1919. He first assisted Dr. Franklin S. Newell and later succeeded him as chief-of-staff at the Boston Lying-in Hospital and professor of obstetrics at Harvard Medical School.

The second part of the book concerns the history of the Boston Lying-in Hospital, beginning

*Irving, F. C. *Safe Deliverance*. 308 pp. Boston: Houghton Mifflin Company, 1942.

in the earliest days of its existence, more than a hundred years ago, under the guidance of Walter Channing. To him are credited two outstanding contributions to medicine—his description of the anemia that occasionally complicates pregnancy and, of more importance, his introduction of anesthesia in childbirth. Here the story is especially well done, and each chapter is full of enlightening and often amusing anecdotes. Channing was followed, after an interval, by David H. Storer and later by his son, Horatio R. Storer. Both were outstanding obstetricians and contributed greatly to the knowledge of the art. The watchword of the first Storer, "Patience and expectancy up to the proper time for interference: prompt and fearless action when that time comes," should, as Dr. Irving notes, adorn the walls of every delivery room and lying-in chamber. To the second Storer should go the credit for the first operation to remove the uterus at the time of cesarean section, performed in 1868, eight years before the classic monograph by Porro, of Milan. Storer, like Long in the ether controversy, failed to realize the significance of what he had done, and his contribution was lost in the passing of time. Later came William L. Richardson and a host of others who kept the name of the Boston Lying-in Hospital at the front in the advancement of obstetrics in America.

Finally there are chapters on general topics: puerperal fever and the importance of Oliver Wendell Holmes's contribution to the subject, first published one hundred years ago this April; the matron of the hospital, Mrs. Higgins, who served from 1873 to 1914; midwifery in general; abortion, therapeutic and otherwise; puerperal convulsions; cesarean section; legitimacy; and the modern practice in obstetrics.

Throughout the book are notes on the teaching of obstetrics in Harvard Medical School and, indeed, important contributions to general knowledge concerning the teaching of the whole subject of medicine. There are many quotable passages: for example, "The most effective teacher is not the colorless intellectual virtuoso who today

deals out as a fact what tomorrow may prove to be only a fancy, or who pursues some petty experimental project; but he is the real doctor who transmits to his pupils the heritage of truth, courage, and kindness that will make his spiritual heirs worthy members of the medical profession."

The book is carefully written and surprisingly full of factual historical material, while enough lightness is given on each page so that a layman may read with both understanding and pleasure. The omission of an index cannot be overlooked, and a chronological tale of events and persons connected with the Boston Lying-in Hospital as an appendix would have greatly aided the average reader.

This is one of the best autobiographies of a doctor published in recent years. Every physician in New England will be delighted with the story unfolded by Dr. Irving. There is plenty of local color, and occasionally a pungent statement, but nothing at any time that will raise a blush in the most fastidious cheek. To the physician outside of the sphere of events ordinarily encompassed by the Boston Lying-in Hospital, this book will be welcome, for in it he will find a rich store of wise comments by a man of broad vision, particularly interested in life, and at the same time a practical, earnest, up-to-date leader of medicine.

MEDICAL EPONYM

STEENSEN'S DUCT

Niels Steensen (1638-1686) was born a Danish Protestant, studied medicine, gave up scientific investigation at the age of thirty-five, and died a Catholic priest at the age of forty-eight. He wrote under the Latinized form of his name Nicolaus Stenonis, and is often called Steno under the misconception that this is the nominative form of the supposed genitive Stenonis. The following account of his discovery of the parotid duct is taken from a letter to Thomas Bartholin, dated Leyden, April 22, 1661, and appears in the first volume of *Nicolai Stenonis Opera Philosophica* (Copenhagen, 1910: pages 3-7). The discovery was made in Amsterdam on April 7, 1660, while Steensen was a pupil of Gerard Blaes, director of the Town Hospital. A portion of the translation follows:

It is now a year since I, having become the recipient of Blasius's hospitality, and marking in that acquaintanceship—to which he put an end the third week after my arrival—a convenient opportunity for studying anatomical subjects, begged the famous man to allow me to dissect with my own hand whatsoever things I should be able to gather together for myself. Having obtained this permission, I was so favored by fortune that in the very first thing which I began to dissect alone—a sheep's head that I had bought at Museolus on April 7—I discovered a duct which, so far as I know, had never yet been described by anyone. I had removed the usual covering layers and was contemplating the dissection of the brain, when by chance I decided to examine first the vessels of the mouth. And so, to this end exploring the courses of the veins and arteries by inserting a probe, I noticed that the point, when driven but a short way in between the narrow layers, wandered around quite freely in a spacious cavity, and soon, when I pushed the metal probe farther, I heard the sound of it against the teeth themselves.

Struck by the novelty of this, I summoned my host to hear what he thought about it: he first began to accuse me of using force, then to resort to the explanation that it was one of Nature's many tricks, and finally turned to consult Wharton. But he could find nothing there either: and since the carelessness with which I had treated the vessels did not allow a more extensive examination, I resolved to repeat this investigation with greater care; and this I did a few days afterward, using a dog's head, although the results were not so clear. Since, therefore, the use of the vessels was proved by the similarity existing between large and small, I sent word in that same month to my close friend, the excellent Master Jacob Henry Paul, telling him that I had found a certain salivary vessel, and appending thereto some sort of description of it. Since, however, I knew that something similar to this had already been previously discovered, and was unable to learn whether or not it was the *same* thing that had been noted by others, I kept silence, until an opportunity presented itself to consult the great Sylvius on the matter. He, on learning my story, resolved to conduct an investigation, using a human body, and finding my story to be true, demonstrated it on numerous occasions in the presence of observers.

You have here, illustrious Sir, the history of the discovery. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

MISCELLANEOUS

During 1941 there were two fatal cases of pernicious vomiting. One of these was that of a woman who had two living children. In this, her third pregnancy, she reported first to her physician six weeks after the last period. At that time she had severe vomiting. She was treated at home for ten days with some improvement but was finally sent

to the hospital because of a return of the vomiting. The blood pressure on admission was 90 systolic, 60 diastolic, and the pulse 130. The urine contained large traces of albumin. The patient was jaundiced. For ten days she was treated conservatively, but continued to go downhill; at the end of that time the nonprotein nitrogen was 117 mg., and the urea nitrogen 51 mg. per 100 cc. A consultation was held, and an abortion was advised; but so far as can be made out from the record, the patient died without operative interference. It is difficult to understand how a patient could, under such close medical care as this, have been allowed to die without operative intervention unless certain scruples contraindicated this procedure. Medically speaking, this was an entirely unnecessary death.

The second patient was a twenty-four-year-old primipara, who at the beginning of the pregnancy apparently had a pyelitis. This was treated in a hospital and cleared up. Excessive vomiting, described as pernicious, developed, and abortion was advised. Abortion was accomplished by packing the cervix. The entire fetus was expelled spontaneously. The temperature rose to 104°F. that evening, and the patient died within forty-eight hours of delivery. As fever developed the night following the operation, it was apparent that the operation was the cause of the infection. No autopsy was obtained, but one can attribute this unnecessary death solely to infection following an operation for pernicious vomiting.

There were two cases in which shock and, probably, hemorrhage were responsible for death. The first was that of a patient who had had one early miscarriage. The second pregnancy was normal in its prenatal course. The patient had a rather long labor. Delivery was accomplished, after forceps had failed, by version and craniotomy. The patient lived about an hour after delivery. There was no transfusion. There is little to be said about this case except that it was handled poorly and that the patient should undoubtedly have had a cesarean section. When one has to resort to version, because forceps-delivery is impossible, it is evident that a mistake has been made. And although there was considerable bleeding in this case, the prolonged operative procedure undoubtedly caused the shock that resulted in death.

The second case was that of a multipara who had three living children. She entered the hospital because of a mild hydramnios and albuminuria. Labor was induced with castor oil and rupture of the membranes, but did not proceed satisfactorily. It is evident that the cervix had not softened and was not amenable to induction by this method. After twenty-eight hours of labor a Waters's extra-

peritoneal cesarean section was done because it was believed that a Brindley ring had formed. The baby weighed 10¼ pounds. The patient was transfused eight times but died four hours later of hemorrhage and shock.

Two patients died of cerebral hemorrhage. On one of these the history is incomplete. At seven months it is said the patient had a cerebral hemorrhage and succumbed undelivered. The second patient had been treated for hypertension for two years. When eight months pregnant a cerebral hemorrhage resulted in paralysis of the right side. She was admitted to the hospital and died three weeks later, undelivered. A post mortem cesarean was immediately performed, and a 5 pound living child was secured. The only sure way to have eliminated this fatality was to have prevented pregnancy.

There were two cases in which, after investigation, the direct cause of death could not be determined. The first case was that of a woman who had had six previous normal pregnancies, the children were living and well. When seven months pregnant, while at a children's clinic, she fainted and was unconscious for an hour. She was immediately sent to the hospital in extreme shock. There was no bleeding and no abdominal spasm, the pulse was 150, no fetal heart could be heard. She started labor ten hours later and delivered a still born baby. Since there was no hemorrhage or excessive clots associated with the birth of the baby, premature separation of the placenta can be ruled out. During convalescence she vomited frequently but gradually improved. Suddenly an attack similar to the initial attack, with unconsciousness and pain in the epigastrium, occurred, from which she did not recover. Unfortunately, no autopsy was performed. Because of the rapid pulse and because of the pain in the abdomen and vomiting, it seems likely that a viscus ruptured. The second case was that of a woman in her fourth pregnancy who had had three previous cesarean sections. This pregnancy was terminated by a cesarean section at term. Spinal anesthesia was given. A minute after pituitary extract had been given, the patient had difficulty in breathing and a tickling in the throat. She suddenly became pulseless, and no blood pressure could be obtained. The pulse returned, but an hour and a half later, laryngeal spasm developed and she again became pulseless. Death followed almost immediately. No autopsy was performed, but it is possible that a hypersensitive response to pituitary extract was the cause of this catastrophe.

There were two cases of suicide. In one of these, the patient at term, arrived at the hospital dead, she was at term but not in labor. The cause of

death was ascertained to be poisoning from drugs. The second case occurred in a primipara, who shot herself through the head, undoubtedly while mentally deranged.

MISCELLANY

RESUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR NOVEMBER, 1947

DISEASES	NOVEMBER 1947	NOVEMBER 1941	PER CENT AVERAGE
Acute poliomyelitis	2	10	5
Cerebral malaria	969	117	1035
Scarlet fever	6	14	16
Diphtheria	583	687	67
Infectious mononucleosis	30	46	48
Cerebral meningitis	67	59	33
Cerebral pneumonia	38	337	422
Neisseria meningitidis	103	457	635
Neisseria meningitidis (serotype 1)	13	14	6
Meningococcus (other forms)	6	7	1
Typhoid fever	639	997	300
Paratyphoid fever	7	5	5
Shigellosis	234	193	264
Amoebiasis	883	734	486
Trachoma	535	397	455
Unidentified	239	199	200
Leishmaniasis	20	23	21
Wuchereria bancrofti	0	2	6
Urticaria	0	5	4
W. bancrofti	900	710	626

* Includes cases for preceding five years.
† Includes men, its only other form reportable previous to 1941.

Actinomycosis was reported from Springfield, 1, total 1.

Anterior poliomyelitis was reported from Fitchburg, 1, Lynn 1 total 2.

Anthrax was reported from Lynn, 1, total, 1.

Diphtheria was reported from Boston, 2, Lowell, 3, Springfield 1 total 6.

Dysentery bacillary, was reported from Cambridge, 1, Camp Edwards 1 Fall River, 5 Waltham (Walter E. Fernald State School), 5, Wrentham (State School), 18, total 30.

Encephalitis, infectious, was reported from Everett, 1, total, 1.

Malaria was reported from Camp Edwards, 1, Middleboro 1 total 2.

Meningitis, meningococcal, was reported from Boston, 2 Cambridge 1 Camp Edwards, 1, Dracut, 1, Fort Branks, 2, Lowell 1 Milton 1 Norwood, 1, Randolph, 1, Stoneham 1 Wilmington, 1, total, 13.

Meningitis other forms was reported from Boston, 1, Cambridge, 3 Fitchburg 1, Worcester, 1, total 6.

Paratyphoid infections were reported from Boston, 2, Lowell 1 Newton 2, Salem 1, Worcester, 1, total, 7.

Septic sore throat was reported from Attleboro, 4 Beverly, 1 Boston, 3, Braintree, 1 Fall River, 1, Fitchburg 1 Quincy, 2, Worcester, 1, total, 14.

Trachoma was reported from Boston, 1, Norwood, 1, total 2.

Typhus fever was reported from Camp Edwards, 1, total 1.

Although the usual high seasonal levels characterize certain of the communicable diseases for November, there were two outstanding exceptions. Typhoid fever, for the first time since the disease was made reportable, is conspicuous by its absence no cases having been reported during November. Undulant fever, too, was not reported.

Preventive Medicine in Modern Practice. Edited under the auspices of the Committee on Public Health Relations of the New York Academy of Medicine. By James A. Miller, Sc.D., M.D., D.P.H.; George Baehr, M.D.; and E. H. L. Corwin, Ph.D. Third edition. 4°, cloth, 851 pp., with 22 illustrations and 37 tables. New York: Paul B. Hoeber, Incorporated, 1942. \$10.00.

This is not a textbook of preventive medicine, but "an attempt to combine in one volume the clinical and environmental aspects of health problems in a manner suited to the needs of both the general practitioner and the specialist." The defect most obvious in such a synthesis is well expressed by one of the fifty distinguished co-authors, Dr. Edgar van Nuys Allen, who contributes the chapter on degenerative diseases, "In the light of present knowledge there is too little fact and too much fancy, too little evidence and too much opinion, and too little knowledge and too many questions."

The book is divided into four sections: sociobiological aspects, clinical aspects, environmental aspects and organizational aspects. It is inevitable that there should be considerable variation in the quality of the many chapters. Of outstanding interest and value are the following: "The Prevalence of Disease," by Haven Emerson; "Tuberculosis," by James A. Miller; "Heart Disease," by Paul D. White and "Provision for the Care of the Sick," by Ray Lyman Wilbur.

It can be heartily recommended to the practitioner of medicine as a means of orienting himself in a field that is certain to be invaded in progressively larger numbers by an army of zealots who will seek to dominate it by legislative and political measures. It is not recommended as a satisfactory text for medical students.

History of the School of Nursing of the Presbyterian Hospital, New York: 1892-1942. By Eleanor Lee, A.B., R.N. 8°, cloth, 286 pp., with 58 illustrations. New York: G. P. Putnam's Sons, 1942. \$3.50.

This is an excellent history of the development of the nursing school in one of the leading hospitals in the country. Of particular value are the illustrations. Miss Lee seems to have found many of them, and not a few may be considered unique. There is, for instance, an excellent picture of the operating theater in 1903, and another showing the parade of the American nurses in Paris on July 4, 1918. This is a book, therefore, that will have an appeal far beyond the average history of a hospital nursing corps. It is a historical document of considerable importance and should find its way into all medical libraries, as well as into the hands of physicians interested in medical history.

Standard Radiographic Positions. By Nancy Davies, M.S.R., and Ursel Isenburg, M.S.R. 8°, cloth, 136 pp., with 103 illustrations. Baltimore: The Williams and Wilkins Company, 1942. \$2.00.

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GOVERNMENT'S OBLIGATION IN INDUSTRIAL HEALTH*

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WASHINGTON, D. C.

WE MEET today at a time of revolutionary changes. In the field of industrial health, as elsewhere, the changing conditions are giving rise to new problems, which we must be prepared to face. First there are the changes in the composition of the labor forces. Older men, women, the physically handicapped and, in some industries, veritable youngsters are all going to work. The chairman of the War Manpower Commission has mentioned a working army of upward of 60,000,000. As we approach this number, we must leave out men of Class 1-A or 1-B selective qualifications. There is a distinct probability that we must also leave out the eighteen- and nineteen-year-old boys. These workers, steadily increasing and without the physical adaptation and experienced work-habits of the men who have been called into service, are laboring harder and for longer hours than heretofore. Eight federal agencies—the Maritime Commission, the War Manpower Commission, the War Production Board, the Department of Commerce, the Department of Labor, the War Department, the Navy Department and the Public Health Service—have jointly subscribed to a policy of urging a forty-eight-hour week limit in war plants. This policy is in line with a statement issued by the Public Health Service nine months ago pointing out that industries operating on a twenty-four-hour-a-day basis must take special precautionary measures to minimize the effects of night work and the rotating shift.

Another important change has been brought about by the growth of boom-town conditions in many areas. The three basic essentials of public health—safe water, safe food supplies and proper sewage disposal—are jeopardized, especially in the more recent industrial and military mobilization areas. Add to this the problems of crowded clinics and hospitals, crowded housing and crowded transportation, and we have a situation that calls for

the best services that our federal, state and local health authorities in combination have to give.

Perhaps the fastest and biggest changes have taken place in our factories. New processes, new machinery, new materials are now in use. Often they have been introduced too rapidly to receive the benefit of investigation from the standpoint of their effect on health. Of course, many of the health hazards are already too well known to call for further research. Welding, dermatosis-producing materials, siliceous dusts, benzol—these four potential occupational hazards come quickly to mind as examples of processes and substances whose dangers we have known for some time. But this easily available scientific knowledge has not been applied in our factories as completely as possible. There is only one way to bridge the gap between knowledge and application. That is by employing trained personnel to do the job. An insufficient supply of trained personnel is one of the great difficulties we have to face in industrial health conservation. Today there are approximately five hundred professionals and technicians in this country trained in the particular complexities of industrial hygiene. Five or six years ago there was hardly one fifth of the present number. Fortunately, the Public Health Service recognized the need at that time. We believed that it was our responsibility to help meet it and to stimulate similar preparation by industry, medicine and professional and technical schools. Each year since 1936 our Division of Industrial Hygiene has run orientation courses for in-service and field training. Without this preliminary start it is doubtful whether we could have handled the sharp upswing of demands for industrial-hygiene services—demands that were motivated largely by the conditions I have just described.

The first big job of the Public Health Service is that of directly assisting the War Department. The Division of Industrial Hygiene has completed surveys of eighty of the one hundred and fifty gov-

*An address given before the Round Table on Health in Industry, Associated Industries of Massachusetts, Boston, October 29, 1942.

†Assistant to the Surgeon General.

Preventive Medicine in Modern Practice. Edited under the auspices of the Committee on Public Health Relations of the New York Academy of Medicine. By James A. Miller, Sc.D., M.D., D.P.H.; George Baehr, M.D.; and E. H. L. Corwin, Ph.D. Third edition. 4°, cloth, 851 pp., with 22 illustrations and 37 tables. New York: Paul B. Hoeber, Incorporated, 1942. \$10.00.

This is not a textbook of preventive medicine, but "an attempt to combine in one volume the clinical and environmental aspects of health problems in a manner suited to the needs of both the general practitioner and the specialist." The defect most obvious in such a synthesis is well expressed by one of the fifty distinguished co-authors, Dr. Edgar van Nuys Allen, who contributes the chapter on degenerative diseases, "In the light of present knowledge there is too little fact and too much fancy, too little evidence and too much opinion, and too little knowledge and too many questions."

The book is divided into four sections: sociobiological aspects, clinical aspects, environmental aspects and organizational aspects. It is inevitable that there should be considerable variation in the quality of the many chapters. Of outstanding interest and value are the following: "The Prevalence of Disease," by Haven Emerson; "Tuberculosis," by James A. Miller; "Heart Disease," by Paul D. White and "Provision for the Care of the Sick," by Ray Lyman Wilbur.

It can be heartily recommended to the practitioner of medicine as a means of orienting himself in a field that is certain to be invaded in progressively larger numbers by an army of zealots who will seek to dominate it by legislative and political measures. It is not recommended as a satisfactory text for medical students.

History of the School of Nursing of the Presbyterian Hospital, New York: 1892-1942. By Eleanor Lee, A.B., R.N. 8°, cloth, 286 pp., with 58 illustrations. New York: G. P. Putnam's Sons, 1942. \$3.50.

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tactics, then, must be to attack the problems of disease from two sides in a combined assault—in the community as well as in the factory.

The venereal-disease clinic, the nursing service, the dental service, the public-health education service, the sanitation section, the maternal and child-health service must reach the industrial worker and his family to a far greater extent than mere routine functions permit. The industrial-hygiene unit has a close, informed relation with management and employees, and therefore is the logical co-operative channel through which these services can reach the worker. The local health department, correspondingly, is the channel through which industrial hygiene can be brought to bear directly on the health problems of workers in small plants. The health officer has at his command the state industrial hygienists, who are trained and equipped to co-operate with him, just as he, by virtue of his position, has the most complete acquaintance with local needs and resources. In this sense, therefore, every division of a state or local health department should play a part in building the foundation for promoting the health of workers. If we agree on the changing nature and extent of our common problems, I think we shall agree that we must prepare for the possibility of changing our methods of dealing with them. As the ratio of physicians to population becomes dangerously low in many areas, we must consider the possibility of industrial doctors' leaving their dispensaries for certain periods of community prac-

tice. If a skilled man is off the job in order to care for his sick wife, it is common sense (as well as enlightened humanitarianism) to treat the woman so that the man can return to war work, where every pair of hands is needed. It would seem that the day is coming when, in many areas, the community physician's practice and the plant physician's patients will have to be handled by *one* and the same man. That man should have—and must have—the co-operation of every governmental agency. He should have—and must have—the understanding and backing of his medical society. He must have the co-operation of the war-production-drive labor-management committees. He must have the same respect, encouragement and attention that top management already gives to operations departments. Last and not least, he must have the friendship and understanding of the workers whom he treats, for only they, in the final analysis, can apply to their daily lives the precepts that he teaches.

All of us, no matter in what field we work, have a single star to steer by. That is the belief that every man and every woman saved from illness or accident is a skill saved as well as a person saved. In the months ahead we shall need every skill, for it is only the total of our many skills on the home front and the battle front that will hasten the final victory. In a changing world, our determination to overcome any and all obstacles through constant effort and teamwork must remain changeless.

THE DIAGNOSIS OF SPRUE IN NONTROPICAL AREAS*

FRANZ J. INGELFINGER, M.D.†

BOSTON

SPRUE and spruelike states are not rare in northern latitudes, but the complicating features are often so prominent that the underlying disorder is not immediately recognized. Four patients seen within the last two years at the Massachusetts Memorial Hospitals illustrate not only the wide variety of symptoms encountered but also the ensuing diagnostic difficulties. In each of these cases initial failure to make the correct diagnosis postponed adequate therapy, which, in sprue, may not be completely curative but will often allow a severely debilitated person to resume a normal life. Hence reports of these patients are presented, not as complete case reports of sprue seen in nontropical areas, but in order to emphasize the secondary phenomena that may be encountered. Excellent descriptions of nontropical and tropical sprue, as well as complete case reports, can be found in the writings of Thaysen,¹ Snell,² Miller and Barker³ and Kantor.⁴

Spruelike states are characterized by steatorrhea, which apparently is not the result of pancreatic disease. Under this heading, tropical sprue, nontropical sprue (idiopathic steatorrhea) and celiac disease of children may be listed. Whether these conditions represent different aspects of the same disease is still a matter of dispute,^{1,2} but for the present purposes, the two adult forms will be considered under the single heading of sprue.

The outstanding feature of this disorder is an excess output of fecal fat, which has led to the conception that the basic abnormality of sprue is a malabsorption of lipids. It is more likely, however, that patients with this disease absorb all substances poorly, even water and gases; and absorption tests using glucose⁵ and glycine⁶ substantiate this conception with respect to sugars and amino acids. On the other hand, the small intestine of man is long enough to compensate for the delayed absorption rate of glucose and amino acids; hence these substances do not appear in the feces to excess. Fats, however, are much more slowly absorbed, even by the normal bowel, and a delayed lipid absorption then causes fatty substances to be spilled into the colon. This, in turn, leads to the fatty stools of sprue. Patients who have had extensive granulomatous disease, resections or short cir-

cuit of the small intestine may also have steatorrhea,⁷ but in these cases the curtailment of the absorbing surface rather than a generalized defect predisposes to the spruelike state. It is then clear that the symptoms of sprue may be predominantly related to the gastrointestinal tract and its disturbed functions; or these symptoms may be minimal, and the patient's major complaint will then be the result of a dietary deficiency conditioned by the poor absorptive capacity of the bowel. Naturally, a deficiency of fatty substances is most likely to occur.

STOOLS

Typically, the patient with sprue has frequent bowel movements consisting of soft, light-yellow, frothy and greasy fecal material. Actually none of the four patients consistently had stools fitting this description during the period that each was under observation, and two never passed stools of this character.

Patient H. S., an unmarried woman, thirty-one years old, of Syrian extraction, complained of gross hematuria of two days' duration. Because she gave the additional history of increasing fatigue, weight loss and hoarseness, the diagnosis of adrenal, laryngeal and renal tuberculosis was entertained. Only on direct questioning did the patient state that she had had an increasing frequency of bowel movements for two or three months. In the hospital, the movements were watery and dark brownish green. The high lipid content of these stools was grossly apparent only after they had been allowed to stand for several hours, when a thick layer of fatty material gradually accumulated on the surface.

Patient W. J., a man of forty-seven, who had been known to suffer from hypocalcemic tetany and from a macrocytic anemia moderately resistant to liver-extract therapy for four years, moved his bowels once daily and occasionally took mineral oil for constipation. Though he had no diarrhea, his stools were light and somewhat greasy in appearance. Sprue had not been considered in his case because of the formed character of the feces.

Patient W. C., a man of thirty-six, had the typical stools of sprue on admission, but after four months of treatment, bowel movements occurred only twice daily, one movement being formed, the other watery. Although the fat intake was limited to 25 gm. daily, the stools continued to be light yellow,

*From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine, Boston.

This study was aided by a grant from Brewer and Company, Incorporated, Worcester, Massachusetts.

†Assistant professor of medicine, Boston University School of Medicine; associate, Evans Memorial, and assistant visiting physician, Massachusetts Memorial Hospitals.

suggesting that this color is not necessarily produced by a high percentage of fecal fat

Fat balance studies on all three patients showed that they excreted 42, 25 and about 80 per cent* of their dietary fat, respectively (normal less than 10 per cent is excreted). But it is not necessary to do such laborious studies, in each of

the diarrhea, he suffered from abdominal distention and cramps. Eight months before admission to the hospital, he was awakened at night with particularly severe colic and distention, accompanied by some nausea and vomiting. An emergency operation for intestinal obstruction was done, but the laparotomy revealed no local lesions, merely a

TABLE 1 Results of Significant Laboratory Studies When the Diagnosis of Sprue Was First Made

PATIENT	RBC CELL COUNT X 10 ⁶	HEMOGLOBIN % (156 gm)	HEMATOCRIT %	SPECIFIC GRAVITY	MCV	MCH	MCHC	WHITE-CELL COUNT X 10	SPECKLED ERYTHROCYTES		PATIENT'S HEMOGLOBIN VALUE
									mg/100 cc	mg/100 cc	
W C	7.9 ¹	0	34.8	1.1	3.3	31.3	3.0	3.0	8.0	2.0	30
W J	3.11	66	33.8	1.0 ²	2.8	3.1	8.0	1.0	7.3	2.0	60
H S	7.56	4 ³					16.0		6.1	1.6	19
J M	7.07	33					.3		5.4	1.6	19

*Patients H S and J M were expected to excrete 10 per cent of dietary fat.

these cases, a microscopic study of a fecal specimen stained with sudan III was enough to show the abnormal steatorrhea.

The stools of all these patients were cultured, but no pathogenic intestinal bacteria were identified. A heavy growth of *Parasaccharomyces A (Monilia albicans)*⁸ was, however, obtained from both the feces and the small bowel contents of patient W C. When the patient improved clinically, the *parasaccharomyces* disappeared from the stools, only to reappear when a mild relapse was precipitated by his failure to observe the prescribed dietary and therapeutic regimen. These observations are in accord with the now generally accepted belief that *parasaccharomyces* are secondary invaders, not etiologic agents in sprue.

DISTENTION AND CRAMPS

A well known symptom of sprue is abdominal distention, the result of abnormal accumulations of gas and liquids in the loops of the small and the large bowel. This distention has usually been ascribed to intestinal fermentation, but a better explanation can be found in the marked loss of intestinal tone, which prevents proper propulsion, elimination and absorption of gases. As in the distended bowel behind a partial obstruction, however, deep contraction waves may pass over the distended loops, producing typical abdominal colic. Usually the atonic symptoms greatly exceed those due to the hyperperistalsis, but not always. The combination of atony with occasional hyperperistalsis leads to the unusual intestinal pattern that roentgenologic studies have demonstrated in sprue.^{9, 11}

Patient W C had had intermittent bouts of progressively severe diarrhea for fifteen years. With

generally loose and flabby bowel stained diffusely with a brown pigment (hemofuscin). Nevertheless, an ileostomy was done. Since symptoms suggesting intestinal obstruction persisted, two more ileostomies were performed in a six month period, each ileostomy being placed higher than the previous one, and each being unsuccessful in alleviating the symptoms. Treatment of the sprue, after the diagnosis was finally made, relieved the symptoms promptly. In spite of all measures, however, this relief was not permanent. Occasional cramps and hyperperistalsis occurred but the negative findings at previous operations, as well as careful diagnostic studies with the Miller-Abbott tube, ruled out organic obstruction. An examination of this patient's stool before the first ileostomy would have pointed to the correct diagnosis and a combined diagnostic and therapeutic use of the Miller-Abbott tube^{12, 14} would have shown that the motor disorder was generalized, not local.

ANEMIA

The anemia that attends sprue may simulate that of pernicious anemia or may be hypochromic and microcytic.¹⁵ In these four patients, the variable hematologic characteristics of this disease are well illustrated in that two had microcytic and two macrocytic anemia (Table 1). The picture was complicated in patients H S and J M, however, since both suffered from purpura and had lost considerable blood at the time the diagnosis of sprue was first established.

When the mean corpuscular volume and the mean corpuscular hemoglobin are increased over their normal upper limits (92 cubic microns and 31 gamma gramma respectively), as was the case in patients W C and W J, the differential diagnosis between sprue and pernicious anemia may

*This patient had an ileostomy. Per cent excretion of fat was determined from the fat content of the fecal contents was impossible.

present some difficulties. As a matter of fact patient W. J. had been considered to have Addisonian anemia three years previously, because he had a red-cell count of 2,240,000, a hemoglobin of 55 per cent and gastric achlorhydria. This diagnosis, however, failed to explain the other findings—the disproportionately large abdomen, the attacks of hypocalcemic tetany and the rather disappointing response to therapy with parenteral liver extract. Usually one can expect that a potent preparation of liver will produce a dramatic response in pernicious anemia, particularly if the anemia is severe. In patients with sprue, liver extract also benefits the anemia, but the amount necessary for this result is often two or three times that needed in pernicious anemia, and a complete eradication is difficult to achieve.

TETANY

Each of the four patients had tetany at one or more periods during his or her illness. Usually the carpopedal spasms were recognized for what they were, but in one case (patient W. C.) a physician who failed to recognize that he was eliciting a Trousseau sign chided the patient when the inflation of the sphygmomanometer cuff around the arm produced a painful spasm of the hand and fingers. Even when Chvostek and Trousseau signs were not obtainable, the serum-calcium levels were below normal (Table 1).

Formerly this hypocalcemia was ascribed to the formation of insoluble calcium soaps in the intestine. Studies of the intestinal tract in man show, however, that the pH of the small bowel rarely rises above 7.5,^{16, 17} and in a medium with a pH of less than 8.0 many soaps do not form.¹⁸ Hence the suggestion of Albright and Stewart⁷ that faulty calcium absorption is a secondary result of poor absorption of the fatty vitamin D offers a more reasonable explanation of the hypocalcemia. Thus, for instance, massive therapy with vitamin D will raise the serum-calcium level in patients with steatorrhea.¹⁹ On the other hand, increasing the dietary fat in patients with sprue is followed by an increased output of fecal calcium.²⁰ These facts suggest that both mechanisms may play a part in producing hypocalcemia.

In spite of the low serum-calcium content, none of our patients showed definite osteoporosis of the long bones. The serum-phosphatase levels were normal.

These observations suggest that sprue should be suspected, as well as hypoparathyroidism and advanced renal disease, when evidences of hypocalcemia are found.

BLEEDING TENDENCY

Patient H. S., as already mentioned, entered the hospital with a chief complaint of hematuria, which was ascribed to a tuberculous renal lesion. Three days after the beginning of the hematuria, the patient commenced to bleed from the nose and mouth as well, and huge purpuric areas formed all over the body (Fig. 1). Only then was the cor-

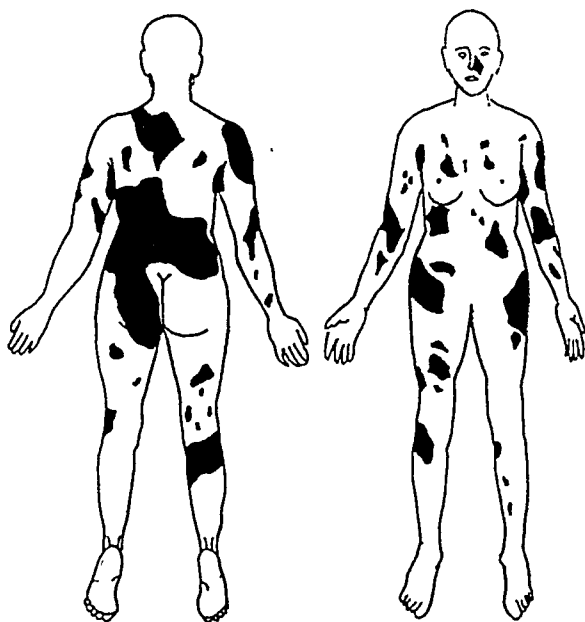


FIGURE 1. *Distribution of Subcutaneous Hemorrhages in Patient H. S.*

rect diagnosis suspected. The prothrombin time had dropped to 1 per cent of normal. Patient J. M.* similarly developed massive purpuric areas within the course of two days, although he had had gastrointestinal symptoms for four years previously. Table 1 gives the prothrombin values in the series.

The cause of the prothrombin deficiency is in all probability the same as that of the hypocalcemia, namely, the failure to absorb a fat-soluble vitamin—in this instance vitamin K. Parenteral injection of the fatty vitamin or oral administration of a water-soluble preparation will immediately arrest the bleeding tendency in these cases. If the diagnosis is not correctly made, the patients may die of internal and external hemorrhages.

VITAMIN A DEFICIENCY

The symptoms of vitamin A deficiency are less dramatic than those of vitamin D or K deficiency, and therefore are often not apparent unless specifically investigated. Two of the patients complained of night blindness, but biophotometer measurements were not carried out. Gross xeroph-

*This case has been reported in detail by Kark, Souter and Howard.²¹

themia was not present. One patient had a dry, scaly skin, but in the presence of an associated deficiency of the vitamin B complex, the significance of this lesion was equivocal. On the other hand, the content of Vitamin A and its precursor, carotene, in the blood can be determined with considerable accuracy.²² Figure 2 shows that the

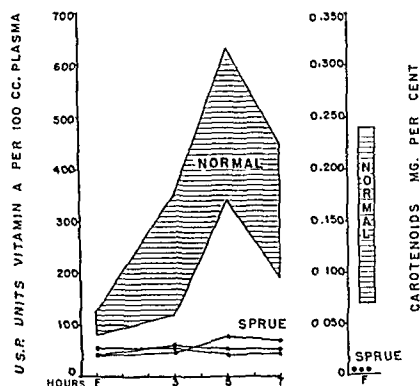


FIGURE 2. Vitamin A Absorption Test and Carotenoid Level in Sprue.

The values in sprue (solid lines and dots) are compared with those in normal persons (shaded area). The fasting figures are indicated at F. The scale on the right shows the fasting carotenoid levels in patients with sprue (three solid dots) and in normal persons (shaded area).

fasting levels of vitamin A in the plasma were strikingly decreased in the 3 patients in whom this determination was carried out, and that carotene was to all intents and purposes completely absent. Furthermore, after a large dose (250,000 international units) of vitamin A was given by mouth, little absorption occurred so far as could be told from the plasma levels. Low vitamin A levels in the plasma and flat absorption curves may, however, be found in other diseases (infections^{23, 24} and hepatic disorders²⁵), and do not necessarily indicate impaired absorption²⁶; but the very low carotene values are particularly significant in establishing the diagnosis of steatorrhea.

VITAMIN B-COMPLEX DEFICIENCY

Patients with tropical sprue often have striking evidence of deficiency of the vitamin B complex, especially of nicotinic acid and riboflavin deficiency. Patient W. C., who had had sprue for fifteen years, was the only one of the patients who exhibited these signs. Cheilosis, angular stomatitis and a dark-red and smooth tongue were promi-

nent. Also striking was the deep, fiery-red color of the mucosa of the proximal and distal portions of the ileum at the site of the ileostomy. Oral administration of 9 mg. of thiamin hydrochloride, 300 mg. of nicotinic acid, 5 mg. of riboflavin and six tablets of Brewer's yeast daily had no apparent effect on the oral and mucosal changes. When thiamine hydrochloride was given parenterally (10 mg. three times a day intramuscularly), an acute exacerbation of the stomatitis occurred. Within one week, the tongue became purple, multiple aphthous ulcers appeared, and the patient had to be given anesthetic mouthwashes for relief. Thereupon he was given parenterally a preparation of vitamin B complex said to contain 3 mg. of thiamine hydrochloride, 10 mg. of nicotinic acid amide, 0.5 mg. of riboflavin, 0.45 mg. of pyridoxine and 1.68 mg. of pantothenic acid per cubic centimeter. He received 2.5 cc. of this preparation daily as well as 2.5 cc. of a crude liver extract (1 unit per cubic centimeter). In three days the symptoms disappeared; one week later the tongue was pale and the fissures at the corner of the mouth had healed; and in one month the lingual papillae began to grow. During this time, the mucosa of the ileum became pinker and much less irritated in appearance.

These observations suggest that this patient was unable to absorb the vitamin B fractions which he was given by mouth, or that the oral doses contained insufficient quantities of the necessary materials. Since the oral doses were given over a period of two months, it is more than likely that the buccal and lingual lesions would have responded had this patient's absorption of riboflavin and nicotinic acid been adequate.

The other three patients had no gross evidence of impaired absorption of the vitamin B complex. This difference was probably quantitative, not qualitative; that is, patient W. C. had by far the greatest absorption defect in respect to all substances and had suffered from this defect for the longest period of time.

CLUBBED FINGERS

Manson-Bahr²⁷ mentions clubbing of the fingers as an occasional finding in nontropical sprue. Patient W. J. exhibited these digital changes. Since this sign has also been observed in patients with ulcerative colitis,²⁸ it appears that chronic malfunction of the intestine may be considered as one of the causes of clubbed fingers.

SUMMARY AND CONCLUSIONS

When sprue and spruelike states are encountered in nontropical areas, the classic features of tropical sprue may be absent or may be obscured

by the secondary nutritional disturbances of the disease. On the basis of observations made on four cases, it appears that the stools are not always numerous or greasy on gross inspection. The disorganized motor activity of the intestines may occasionally produce symptoms suggesting organic intestinal obstruction. In other patients, the gastrointestinal symptoms play a secondary role in the clinical picture, which may be featured by tetany, a generalized bleeding tendency or anemia. Vitamin A and particularly carotene are present in low concentrations in the plasma, and night blindness is at times noticed. Evidences of a deficiency of the vitamin B complex, such as stomatitis and glossitis, are not always found, especially in the nontropical variety of sprue. Occasionally digital clubbing is observed.

The diagnosis of sprue in these four cases was made respectively eight months, three years, four years and fifteen years after the onset of symptoms. This delay may be ascribed to the facts that this diagnosis is not considered in northern climates and that the typical picture of sprue may be obscured by such features as have been described. The diagnosis, once thought of, is not difficult to make, a simple sudan III stain of the feces usually being sufficient to determine the presence of steatorrhea. To establish the diagnosis completely, determinations of prothrombin, calcium and carotene in the plasma, roentgenologic studies of the small intestine and, possibly, pancreatic function tests may be necessary. In most cases, however, the clinical picture combining the characteristics of a chronic but noninflammatory intestinal disorder with anemia and evidences of deficiencies of vitamins A, D and K should be sufficient to bring the diagnosis of sprue to mind.

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CASE 2. W. W., a 64-year-old physician, had a history of angina pectoris of 4 years' duration. The pain was brought on by climbing one flight of stairs or walking three or four city blocks, and was relieved by rest or nitroglycerin. He required 2 to 4 nitroglycerin tablets

before precipitating an attack and the pain lasted 23 seconds (Fig. 2).

CASE 3. B. M., a 54-year-old boilermaker, had a history of angina pectoris of 9 months' duration that be-

TABLE 1. Results of Exercise-Tolerance Tests in 4 Patients Treated with Testosterone Propionate (25 mg. per d

PATIENT	No. OF INJECTIONS		TIME		TOTAL No. OF INJECTIONS	DURATION OF THERAPY	No. OF TRIPS*		DURATION OF PAIN	
	BEFORE SUBJECTIVE IMPROVEMENT	AFTER QUANTITATIVE IMPROVEMENT	BEFORE SUBJECTIVE IMPROVEMENT	AFTER QUANTITATIVE IMPROVEMENT			BEFORE THERAPY	AFTER THERAPY	BEFORE THERAPY	AFTER THERAPY
			days	days					sec.	sec.
E. W.	3	6	14	26	16	87	39	82	169	1
W. W.	3	8	14	32	12	57	39	71	92	1
B. M.	2	6	5	33	10	78	43	76	45	1
J. W.	4	6	14	21	14	63	27	47	72	4

*Trips—average of three tests preceding inception and cessation of therapy.

†Pain—average of three tests preceding inception and cessation of therapy.

daily. The pain was substernal and radiated down the left arm.

Physical examination revealed a blood pressure of 140/70. The heart size was within normal limits, the sounds were fair in quality with a harsh systolic murmur at the base; no thrills were present. The electrocardiogram showed

progressively worse; he had been unable to work 4 months. The pain, which was substernal, was precipitated by the climbing of one flight of stairs or the ingestion of a heavy meal, and was relieved by rest or nitroglycerin.

Physical examination revealed a blood pressure of 100. The heart was not enlarged, and the rate and rhythm were normal. There were no thrills or murmurs, but sounds were distant. An electrocardiogram showed deep Q₃ and late inversion of T₃, suggesting an old anterior myocardial infarction.

The exercise-tolerance test prior to testosterone propionate therapy ranged from 39 to 47 trips and the duration of the pain varied from 35 to 60 seconds. Subject

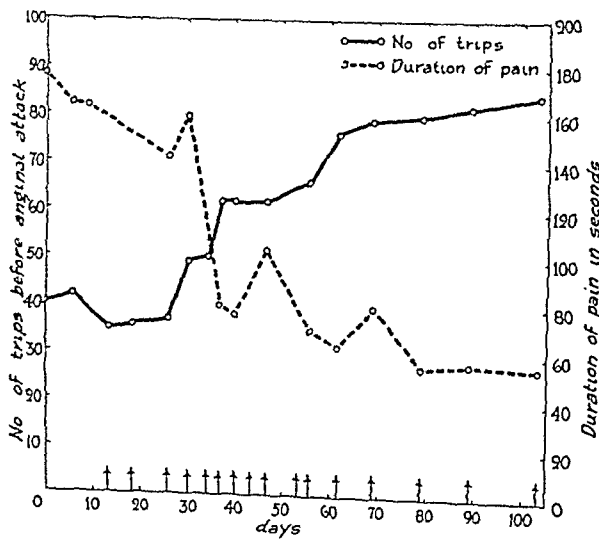


FIGURE 1. Patient E. W.

This and the other three charts (Figs. 2, 3 and 4) show the effects of testosterone propionate therapy on exercise tolerance and the duration of anginal pain. In each chart, an arrow represents one injection of 25 mg. of testosterone propionate.

a high degree of left-axis deviation, and frequent ventricular extrasystoles with runs of bigeminal rhythm. The patient was not taking digitalis.

After only three injections of testosterone propionate the patient reported that he was able to perform his usual duties without resort to nitroglycerin. The exercise-tolerance test, which prior to testosterone propionate therapy required from 32 to 43 trips to produce anginal pain lasting from 90 to 94 seconds, showed definite improvement after the eighth injection. At the end of twelve injections the patient was able to perform 72 trips

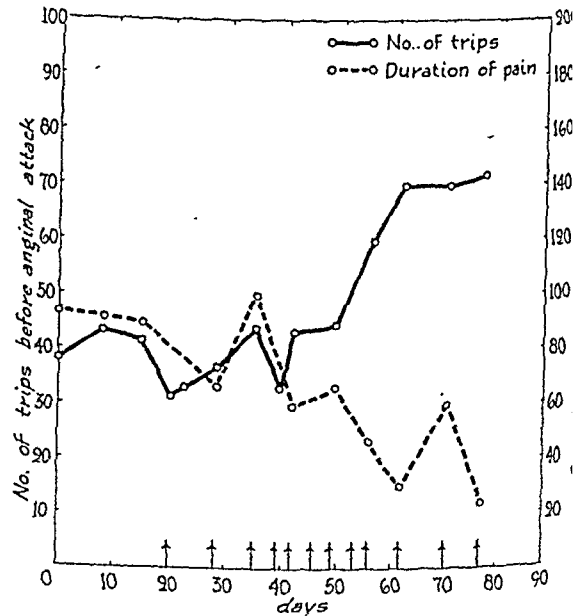


FIGURE 2. Patient W. W.

improvement was reported after the second injection. It was not until after the sixth injection, however, that quantitative improvement was observed. Then the patient was able to make 80 trips before precipitating an attack. The duration of the pain was decreased to as low as 15 seconds

during the period of treatment (Fig 3) After the fifth injection the patient returned to his work on an 8 hour shift and experienced no further attacks

CASE 4 J W, a 60 year old barber, had a history of angina pectoris of 13 years duration Substernal pain

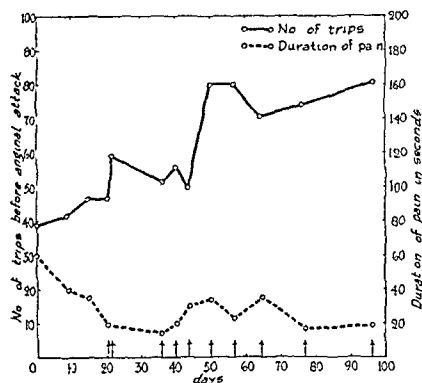


FIGURE 3 Patient B VI

accompanied by numbness of the left hand was precipitated by climbing one flight of stairs or walking two city blocks, and was relieved by rest or nitroglycerin. He required 4 or 5 nitroglycerin tablets daily.

Physical examination revealed a blood pressure of 120/80. The heart was not enlarged and the rate and rhythm

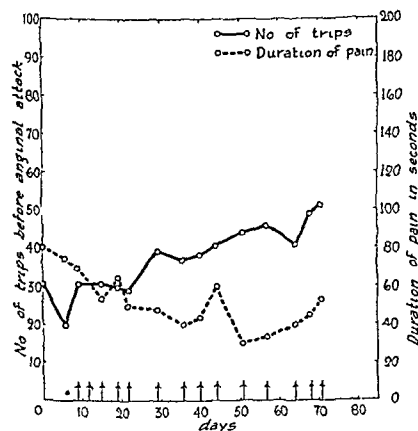


FIGURE 4 Patient J IV

were normal. There were no thrills or murmurs, but the sounds were distant. An electrocardiogram showed a deep Q_1 and late inversion of T_3 suggesting an old posterior myocardial infarction.

The exercise tolerance test prior to testosterone propionate therapy ranged from 20 to 31 trips and the duration of the pain from 70 to 80 seconds. Improvement was reported by the patient after the fourth injection, but it was not until after the sixth injection that quantitative improvement was observed. This reached its maximum after the fourteenth injection, when he was able to make 51 trips before experiencing substernal pain, which lasted 53 seconds. The shortest duration of pain after therapy was 30 seconds (Fig 4). After the sixth injection the patient required only the occasional use of nitroglycerin.

DISCUSSION

The present study provides further evidence of the value of testosterone propionate in the treatment of angina pectoris. This agent not only reduces the frequency of the attacks but decreases their severity when they do occur. It is important, however, to stress that it does not give immediate relief from an anginal attack, as does nitroglycerin. Furthermore, the improvement after the use of this drug varies with the individual patient both in time of onset and in degree. Whereas some patients in this series showed improvement after the second or third injection of testosterone propionate, there were others in whom no improvement was noted until the eighth, ninth or even tenth injection. Again, some patients required as many as fifteen to twenty-five injections over a period of months before therapy could be discontinued. These considerations emphasize the importance of individualizing each case and of giving an adequately long course of treatment. It seems doubtful whether giving the drug more frequently would produce more favorable results, since the time element plays such a significant role in obtaining the desired effect. This is borne out by the results obtained in the group of patients reported here. An average of twenty-eight days elapsed before quantitative improvement was noted, and a period of forty-three days elapsed before this improvement became marked. Although it is recognized that spontaneous improvement may occur in some patients with angina pectoris over the course of weeks or months, it would be most unusual for this improvement to occur uniformly in a large series of patients in such a short space of time.

Since the beginning of the present study, not enough time has elapsed to determine the duration of the beneficial effects of testosterone propionate therapy. In the previous study¹ it was noted that this period varied with the individual patient. The shortest period of benefit was two months, whereas the longest period that a patient has been free of anginal attacks is eighteen months. It is significant that those patients who returned for further treatment because of a recurrence of pain reported that their attacks were less severe than originally, and furthermore it was found that fewer injec-

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			days	days					sec.	sec.
E. W.	3	6	14	26	16	87	39	82	102	51
W. W.	3	8	14	32	12	57	39	71	92	5
B. M.	2	6	5	33	10	78	43	76	45	21
J. W.	4	6	14	21	14	63	27	47	72	1

*Trips—average of three tests preceding inception and cessation of therapy

†Pain—average of three tests preceding inception and cessation of therapy.

daily. The pain was substernal and radiated down the left arm.

Physical examination revealed a blood pressure of 140/70. The heart size was within normal limits, the sounds were fair in quality with a harsh systolic murmur at the base; no thrills were present. The electrocardiogram showed

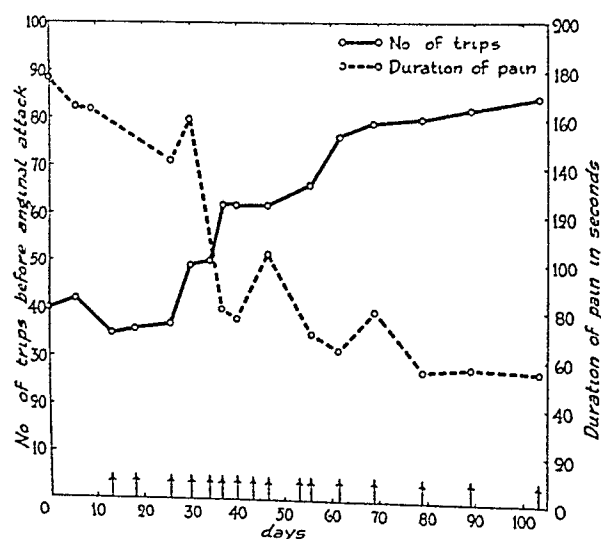


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progressively worse; he had been unable to work for 4 months. The pain, which was substernal, was precipitated by the climbing of one flight of stairs or the ingestion of a heavy meal, and was relieved by rest or nitroglycerin.

Physical examination revealed a blood pressure of 100/75. The heart was not enlarged, and the rate and rhythm were normal. There were no thrills or murmurs, but the sounds were distant. An electrocardiogram showed a deep Q₃ and late inversion of T₃, suggesting an old anterior myocardial infarction.

The exercise-tolerance test prior to testosterone propionate therapy ranged from 39 to 47 trips and the duration of the pain varied from 35 to 60 seconds. Subjective

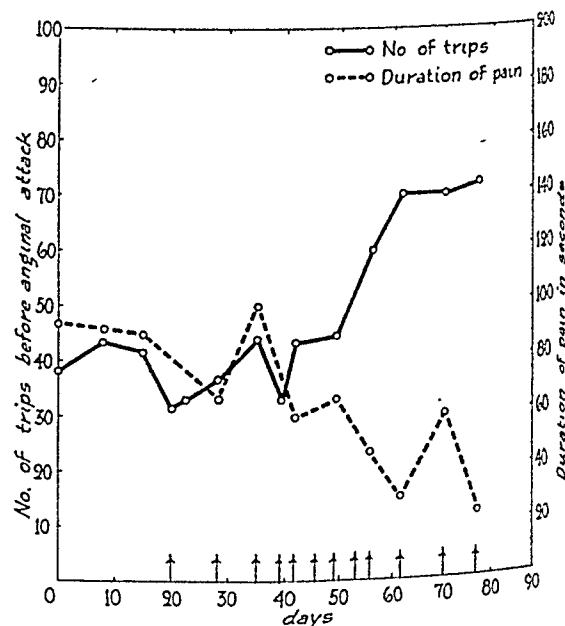


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improvement was reported after the second injection. It was not until after the sixth injection, however, that quantitative improvement was observed. Then the patient was able to make 80 trips before precipitating an attack. The duration of the pain was decreased to as low as 15 seconds

sidered, more recent articles by Bomford and Rhoads⁵⁶ present careful studies of this tissue. The term "refractory anemia" is in some respects unfortunate because it emphasizes refractoriness to therapy rather than the diverse etiologic and pathologic changes that are present. In my own experience, it is of distinct importance to determine the status of the marrow, the possibility of hepatic, splenic or thyroid disease, the presence or absence of a hemolytic process and the possibility of a disorder of fat metabolism, such as Gaucher's disease. Despite the reduction of red cells, white cells and platelets in the blood, the bone marrow at biopsy may be extremely cellular. Leukemia — myelogenous, lymphatic or monocytic — shows extreme leukocytic proliferation; lymphosarcoma and Hodgkin's disease may show the characteristic cellular proliferations of these diseases; and carcinoma may show neoplastic cells. Fibrosis, aplasia and so forth may be readily seen and Gaucher cells are quite easily recognized. From the standpoint of prognosis and possible therapy, it is important to discriminate between these conditions, and the sternal bone-marrow biopsy, whether performed by simple puncture — which is adequate in most cases — or by trephine, is pre-eminent in this regard. Myxedema should not be forgotten as a cause of refractory normocytic anemia, and I have seen a number of these cases treated for various blood conditions. Hepatic disease, particularly with splenomegaly, or various conditions in which splenomegaly is prominent — splenic-vein thrombosis, Gaucher's disease and even certain cases of hypersplenic hemolytic anemia — may result in pancytopenia. Splenectomy may be of definite value in such cases in restoring the blood picture to normal levels.

"Pancytopenia" is perhaps a better term than "refractory anemia" because it indicates simply that the cells in the blood are all reduced. In any event, one should realize that the finding of these hematologic abnormalities is merely a point of departure for further careful studies, which may include the marrow, the liver function, the basal metabolism, the urobilinogen excretion and so on. Pancytopenia, like anemia, is merely a symptom that requires clarification before a definite diagnosis can be determined.

The therapy of aplastic anemia, and in fact of most of the cases showing pancytopenia, — except those in which myxedema, splenic disease or increased hemolysis can be demonstrated, — is admittedly unsatisfactory. Vaughan⁵⁴ tried sternal bone-marrow transfusions in 4 cases of aplastic anemia with completely negative results. I have had similar experiences in both adult and juvenile aplastic anemia. Congenital hypoplastic anemia

of infancy and childhood is a definite entity in which there is a congenital failure of erythropoiesis. These children may be kept alive and well indefinitely by repeated transfusions. Splenectomy is of questionable benefit, but may be valuable if there is any evidence whatever of increased blood destruction. Kohlbr²⁷ found no effect from sternal bone-marrow transfusion. The value of this procedure,⁵⁸ in which a few cubic centimeters of normal sternal marrow admixed with blood is placed in a patient's sternal-marrow cavity, must be seriously questioned.

HEMOLYTIC SYNDROMES

Familial Types

A classification and a discussion of the mechanisms of the hemolytic syndromes were presented in last year's review.⁵⁹ In an American Medical Association exhibit, Dameshek, Greenwalt, Tat and Dreyfus presented in graphic form the physiologic, etiologic and clinical aspects of the various hemolytic syndromes, including the familial and acquired hemolytic anemias and the hemoglobinurias.* There are three types of familial, hereditary hemolytic anemias: spherocytic, Mediterranean target-oval-cell and (African) target-sickle-cell. The spherocytic type is familial; ordinarily known as congenital hemolytic jaundice, it responds well to splenectomy. The Mediterranean target-oval-cell syndromes (commonest in Italians and Greeks) vary greatly in their severity from the fatal Cooley's anemia to mild hypochromic anemia with target and oval cells.^{2, 60} One of their characteristic features is the presence of the target cell in increased numbers. Since these cells are thinner than normal, the hypotonic fragility test shows increased resistance. With the target cells are usually found varying numbers of oval or elliptical and heavily stippled erythrocytes. Despite the low color index, which is always present, these cases are completely refractory to iron therapy. They are important diagnostically since icterus, splenomegaly, anemia, stippling of the red cells and even heart murmurs are common. From the hereditary standpoint, they are of unusual interest since inheritance is Mendelian dominant in type, most of the progeny being affected. Of even more significance is the fact that the mating of two individuals with the mild disease may result in severe Cooley's anemia in one or more of the children.

Since target cells and increased hypotonic resistance are common in sickle-cell anemia, and since there are many other features of resemblance with the target-cell syndromes, the possibility was

*This exhibit has been reprinted in book form (*Hemolytic Syndromes* By William Dameshek, M.D., Tibor J. Greenwalt, M.D., Russell F. Tat, M.D., and Carlisle Dreyfus, M.D. 43 pp. Boston: The Bailey Press 1942.)

advanced that the Mediterranean target-cell disease might be related to the essentially African target-sickle-cell syndromes. Transitional forms between the two syndromes have been found. Heart murmurs, usually rough systolic in type, are noted in both conditions. In a young Negro child it is often difficult to determine whether the murmur is of rheumatic origin or due to the sickle-cell anemia. Spells of fever and joint pains are common in both conditions, and it is therefore necessary in every case to rule out sickle-cell anemia and the sickling trait. These points are discussed by Walker and Murphy⁶¹ and by Klinefelter.⁶² The former authors report an unusual case in which sickle-cell anemia was complicated by acute rheumatic heart disease. Klinefelter attributes all the cardiac findings in sickle-cell anemia to diffuse enlargement of the heart with resultant systolic and diastolic murmurs and prolongation of the PR interval in the electrocardiogram. Although he believes that the cardiac changes are secondary to the severe long-standing anemia, this often seems unlikely since the murmurs are often very striking and the anemia very mild. What is more, cases of severe hypochromic, hemolytic and pernicious anemia usually fail to show murmurs of such degree of severity.

Familial hemolytic jaundice should be differentiated from a familial nonhemolytic variety that was recently described by Dameshek and Singer.⁶³ Although the jaundice is familial, hereditary and acholuric, and associated with the presence of indirect bilirubin in the blood, there are no evidences of increased blood destruction. There is no splenomegaly, and the blood-cell and reticulocyte counts are normal. The bile-pigment output as measured by the fecal urobilinogen is low. Why, then, the jaundice? This appears to be due to a constitutional hepatic dysfunction, the liver cells being unable to remove bilirubin from the blood stream at a normal rate. Thus there seems to be a specific physiologic dysfunction in bilirubin excretion, since other liver-function tests are completely negative and biopsy of the liver is normal.⁶⁴ The incidence of this disorder is much higher than has been suspected. Many cases of mild jaundice probably fall into this category.⁶⁵ The importance of the condition lies in the fact that it is commonly mistaken either for familial hemolytic jaundice or for hepatic disease. Other than diagnostically, it appears to have no great significance, since a number of persons in these families have been known to reach old age.

Acquired Types

The results of splenectomy in the hemolytic crisis of familial spherocytosis are as a rule excel-

lent, but there is still disagreement regarding its value in the acute cases of the acquired groups. Thus, Sharpe and Tollman⁶⁶ in describing 5 cases of "refractory hemolytic anemia" found that transfusions produced dangerous and alarming reactions in 2 cases and that splenectomy in each case failed to modify the course of the disease. The latter statement is not borne out by the case reports. Thus, in Case 1 the patient slowly recovered after operation, whereas prior to it the course had been progressively downhill. Case 2 was obviously not one of hemolytic anemia (no anemia, normal reticulocyte count, direct bilirubinemia and so forth). In Case 3, in which the patient was desperately ill, there was prompt improvement in the blood and progressive decrease of the jaundice with slow but complete recovery. In Case 4, the diagnosis of hemolytic anemia must be considered as extremely doubtful, since there was no record of bilirubin estimation, the reticulocyte percentage was only 2.4 per cent, and the leukocyte and polymorphonuclear counts were very low. In Case 5, splenectomy was postponed until the hemoglobin percentage was 16, and the red-cell count 510,000! It was then performed as an emergency measure and the patient died shortly afterward. Thus of the five so-called "refractory cases" reported, 2 may not have been hemolytic anemia, in 2 the patient recovered, and in 1 procrastination may have been at least partly responsible for the poor result.

Jackson, Parker and Lemon⁶⁷ claim that some cases of "agnogenic" (idiopathic) myeloid metaplasia of the spleen masquerade as hemolytic anemia and that it is important not to remove the spleen because blood cells are being produced there. However, in hemolytic anemia it can be shown that the bone marrow is extremely hyperplastic in response to hemolysis and that myeloid metaplasia of the spleen and liver is a frequent occurrence. Brewster and Wollenman,⁶⁸ apparently accepting Jackson's viewpoint, have recently reported a case of acute acquired hemolytic anemia with spherocytosis in which splenectomy was unsuccessful. The myeloid metaplasia is stressed and the intimation is made that this case probably belongs in Jackson's group. I have seen marked myeloid metaplasia both of the spleen and liver in patients who have recovered after splenectomy, and this is not surprising in view of widespread regenerative activity in response to hemolysis.

My own conception of the value of splenectomy in acquired hemolytic anemia is based on a study of 18 splenectomized cases, of which 10 made full recoveries and 8 died.⁶⁹ Although this mortality rate is undoubtedly high, it included a number of procrastinated and desperate cases. In these cases, the high mortality with splenectomy (about 40

per cent) must be balanced against the almost certain 100 per cent mortality involved in the policy of "waiting for something to turn up." It is quite impossible in a given case to state categorically whether or not recovery will take place; however, it is unwarranted to withhold operation, which may prove dramatically successful. Temporization, which involves many transfusions, may result in irreversible hemolysis for which splenectomy is often valueless. If the patient fails to respond to two or three transfusions, splenectomy should be done.

One of the acquired hemolytic anemias in which splenectomy has no effect is that curious condition known as paroxysmal nocturnal hemoglobinuria. In this disease, there are chronic hemolytic anemia, persistent hemosiderinuria and paroxysms of nocturnal hemoglobinuria. The mechanisms are completely obscure. The red cells of this disease are unusually susceptible to hemolysis by dilute acid and the acid fragility test therefore becomes of great importance in the diagnosis of an acquired case in which hemoglobinuria may not be prominent. Both why the red cells are broken down in intravascularly (only in the kidneys?) and why hemosiderinuria is always present are mysteries. Experiments that may have a bearing on some of these points are presented by Yuile, Steinman, Hahn and Clark.⁷⁰ These authors noted a drop in the renal threshold for hemoglobin in dogs after repeated injections, together with dense deposits of iron staining pigment in the convoluted tubules—findings that are present in the above disease. These and other data are summarized in a review article on hemoglobinuria by Yuile.⁷¹

Methods

By the use of the Evelyn photoelectric colorimeter, it is possible to differentiate readily and quantitatively between the prompt (direct) bilirubin and the delayed (indirect) type. Lefebvre⁷² and Cantarow, Wirts and Hollander⁷³ have investigated these phenomena. Cantarow et al. recommend the quantitation in each case studied of both indirect and direct bilirubin, since if the direct bilirubin is increased either absolutely or relatively, it indicates some degree of hepatic impairment. The use of the bile pigment output, chiefly the fecal urobilinogen, and of the hemolytic index in the measurement of hemolysis is stressed by Miller, Singer and Dameshek.⁷⁴ These observers state that of the various indexes of possibly increased hemolysis—icteric jaundice, indirect bilirubinemia, an increase in the urinary excretion of urobilinogen, anemia and leukocytosis—no one is specific. An increase in the daily fecal output of urobilinogen or in the hemolytic index is, however, unequivocal evidence of an increased

breakdown of blood. The latter index relates the output of bile pigment to the total grams of circulating hemoglobin from which the urobilinogen is derived. Thus the output of 200 mg of daily fecal urobilinogen at a level of 5 gm of hemoglobin per 100 cc of blood represents three times as much destruction as the same output at a 15 gm level. This holds true for children as well. A male adult weighing about one hundred and fifty pounds excretes over 150 mg of urobilinogen. This amount in a fifty pound child represents about three times normal value. The urobilinogen output following transfusions of stored and fresh blood was studied by Wasserman, Volterra and Rosenthal.⁷⁵ The excretion of bile pigment after transfusion with stored blood was far higher than after transfusion with fresh blood, being directly proportional to the length of time of blood storage. Blood stored for more than seven days was so readily broken down that the authors concluded that its use was inadvisable in anemia. According to my own experience, the use of stored or bank blood, however fresh, should be reserved for hemorrhage or shock. For any of the so called 'blood dyscrasias'—whether concerned with the red cells, white cells or platelets—fresh citrated blood is best.

The osmometric behavior of normal human erythrocytes has been studied by Guest and Wing⁷⁶ by the use of an ingenious method in which the degree of actual swelling of the red cells under conditions of hypotonicity could be studied. These experiments indicated that normal human erythrocytes are perfect osmometers, that is, they behave mathematically correctly with reference to swelling in relation to the various hypotonic salt solutions. By means of a radioactive ion technic for tagging the red cells, Cruz, Hahn, Bale and Belfour⁷⁷ reached the surprising conclusion that old cells are far more resistant to hypotonic salt solutions than new cells (reticulocytes). This is contrary to what one might expect physiologically.

HEMORRHAGIC DIATHESSES

Lozner⁷⁸ states. "The body, when injured, possesses two main defenses against the occurrence of hemorrhage. These may be called the blood coagulability defense and vascular defense." The blood coagulability defense may in general be subdivided into two headings, comprising the platelets and the various chemical or enzymatic factors that are concerned in making blood clot when it is shed. Thus three main types of hemorrhagic diathesis may be discriminated: that which is associated with a disturbance in one or more of the chemical factors, such as calcium, thromboplastin, prothrombin, thrombin, fibrinogen, fibrin and antithrombin; that due to a deficiency or defect

of the blood platelets; and that secondary to a disturbance in the capillary walls. The first two may properly be grouped in the blood dyscrasias; the third is a vascular condition.

Methods

Ivy, Nelson and Bucher⁷⁹ describe a standardized cutaneous venostasis bleeding-time technic in which the skin of the forearm is used, venostasis being produced by a pressure of 40 mm. of mercury from a sphygmomanometer cuff. The normal mean bleeding time by this method was 61.56 (\pm 2.08) seconds. To control most of the known factors that influence the bleeding time, Copley and Lalich⁸⁰ devised a so-called "hemorrhagometer," in which the principle of bleeding into fluid kept constantly at 37°C. was used. In addition to the red-cell or blood flow, a whitish flow was observed, which was believed to be mostly lymph, and thus a "lymph time" was suggested. The normal bleeding time by this method was 170 to 180 seconds, which is quite comparable to the Duke bleeding time, in which a simple puncture of the ear is performed. Lozner, Taylor and MacDonald⁸¹ studied the effect of foreign surfaces on blood coagulation. Glass apparently has a definite effect in causing blood to clot rapidly, since the same blood in paraffin-treated or plastic (Lusteroid) tubes shows a far longer clotting time: that is, glass eleven minutes, paraffin forty-four minutes and plastic forty-nine minutes. This difference is probably due to the presence of negatively charged ions on the glass surface. It is fortunate that the capillary endothelial surfaces behave more like plastic than like glass. At any rate, the surface with which the blood comes in contact must also be considered in the blood-clotting problem.

Although Quick's method for determining prothrombin in the blood is almost universally accepted, modifications are constantly being published. It is true, as Quick himself stated, that his and other tests are based on an unproved assumption—namely, that they actually measure prothrombin—and "therefore the validity of the results which they yield can be judged only by correlation with clinical observation." Copley⁸² believes that the term "prothrombin concentration" may be inaccurate and says that the term "prothrombin time" is to be preferred. Cheney⁸³ presents a simplified plasma-coagulation time in which recalcification is carried out but thromboplastin (rabbit brain) is not used. He contends that the addition of thromboplastin is unnecessary and that the test is satisfactory for vitamin K deficiency provided the physical conditions of the procedure are closely adhered to. A "one-minute bedside prothrombin method" is described by Rhorer,⁸⁴ who states that it gives results quite comparable to other more difficult and

time-consuming tests. A large drop of blood is allowed to fall into the hollow of a suitable glass slide, following which thromboplastin is added and the coagulation time observed.

The failure of circulating blood to clot spontaneously in vivo still remains an obscure phenomenon, according to Wilson,⁸⁵ since all the elements essential for immediate coagulation in vitro are apparently present. Howell has consistently maintained that there is an antithrombic substance in the blood. This might be heparin. His views are summarized in his recent article.⁸⁶ Wilson describes a method for the determination of antithrombin in blood serum and plasma and finds that normal blood contains an average of 90 units of this substance per cubic centimeter. He states that the hemorrhagic tendency in hypoprothrombinemia is not fully explained on the basis of decreased prothrombin but that hemorrhage usually occurs when the prothrombin unitage approximates or is lower than the antithrombin unitage. Tagnon⁸⁷ describes a method for obtaining from oxalated plasma a proteolytic enzyme active in blood coagulation. This enzyme appears to play a primary role in the mechanism of blood coagulation and its absence may be the cause of hemophilia.

Bell, Lazarus and Munro⁸⁸ describe a standardized method for the determination of capillary fragility based on Gothlin's method of 1931 and similar to that worked out more recently in this country by Wright and Lilienfeld.⁸⁹ A circle is measured over the forearm and a blood-pressure cuff is inflated over the upper arm for fifteen minutes at 50 mm. The petechiae are counted with the naked eye. A petechial count below eight can be regarded as normal, whereas eight or more petechiae require further investigation. In women near the menstrual cycle and in individuals with diminished ascorbic acid levels, the petechial count may be increased. If these factors can be excluded, a high petechial count is definitely abnormal.

Clinical Features

Hypoprothrombinemia. Sanford and Shmigel'sky⁹⁰ studied in infants the question whether the presence of bile and food in the small intestine is necessary for the formation of prothrombin. They concluded that the present explanation of the synthesis of vitamin K by bacteria in the small intestine and the necessity of bile for its conversion is untenable. The liver appears to be the principal source of this vitamin and continues to form it independently of extrinsic causes until its functions are diminished by serious damage. The chemistry of vitamin K is fully (and readably) discussed by Fieser,⁹¹ one of the leaders in this field. A

rarity, namely a case of idiopathic hypoprothrombinemia in a boy of eighteen, is described by Rhoads and Fitz-Hugh.⁹² The case had previously been classified as an atypical one of hemophilia because of a persistent tendency to bleed. In another article on experimental hypoprothrombinemia, Rhoads, Warren and Panzer⁹³ state that a reduction of plasma prothrombin has been effected experimentally by at least ten different means, including modifications of the diet, the liver and the bile ducts, as well as through sweet-clover disease. Clinically, hypoprothrombinemia may be due to dietary K avitaminosis; to a conditional K avitaminosis secondary to the absence of bile salts from the intestinal tract and to liver injury of sufficient degree to prevent synthesis of prothrombin at an adequate rate. The latter condition does not respond to vitamin K therapy, the first one responds quickly, and conditioned vitamin K deficiency requires bile salts in addition to oral vitamin K.

The administration of vitamin K to women in or just before childbirth has been recommended as a routine procedure. It is well to remember that many newborn infants have a low concentration of prothrombin without presenting any evidence of hemorrhagic disease. If the concentration of prothrombin in the blood can be raised prior to the rigorous journey through the birth canal, it is probable that intracranial hemorrhage and its distressing sequelae can be largely avoided. Mull, Bill and Skowronska⁹⁴ recommend 1 mg. of the vitamin orally, four to ten hours before delivery. Most authors recommend the intramuscular injection of a vitamin K preparation during the first stage of labor, especially since gastrointestinal absorption by the mother may be subject to much fluctuation. Infants of mothers treated with vitamin K usually present a normal prothrombin time, quite in contrast to those from untreated mothers. Infants with clinical evidence of hypoprothrombinemia can be treated with 1 mg. orally at eight-hour intervals for a day.

Knowledge that the hemorrhagic sweet-clover disease of cattle is due to hypoprothrombinemia has led to a series of brilliant investigations, chiefly by Link and his associates of the University of Wisconsin, culminating in the synthesis of 3,3'-methylenebis (4-hydroxycoumarin). This substance, when given orally, produces a well-marked reduction in prothrombin and can thus be used to diminish the coagulability of the blood. Bingham, Meyer and Pohle⁹⁵ and Meyer, Bingham and Axelrod⁹⁶ report on the experimental and clinical aspects of dicoumarin administration. The substance is given orally in an initial dose of 5 mg. per kilogram of body weight, with daily doses thereafter of 1.5 mg. per kilogram. Since individual

responses vary considerably, it is necessary to control the prothrombin and coagulation times frequently. Cautiously used, dicoumarin may be of value in conditions with impending or active thrombosis or following splenectomy. Because of the ever-present possibility of hemorrhage (cerebral, renal and so forth) its present use should be limited to patients kept under carefully controlled observation. Administration of vitamin K will not correct the prothrombin deficiency induced by the drug.

The thrombic activity of a globulin fraction derived from rabbit plasma and the use of rabbit thrombin as a local hemostatic were described by Lozner, Taylor and Taylor⁹⁷ and were mentioned in last year's review. For local use, a square of saline-moistened filter paper is placed over the dry powdered rabbit thrombin (Lederle) that has been applied to the wound. This therapeutic procedure should prove of great value in the control of local bleeding and has even been found effective as a local application to bleeding surfaces. The treatment of the latter disease still remains unsatisfactory, however, chief reliance being placed on transfusions of blood. Johnson⁹⁸ points out that certain difficulties are involved in transfusions, namely the necessity of typing and cross-matching and the possibility of building up intragroup incompatibilities with repeated transfusions. Johnson used dry plasma from blood that had been processed within the first few hours after removal from the donor. Keeping blood for seven days before lyophilization resulted in a very definite reduction in its thromboplastic activity. However, dry plasma that had been kept for months at 5°C. showed no reduction in its clot-promoting property. The average dose of plasma used was 125 to 150 cc.; typing of the plasma was found unnecessary, even with unpooled plasma. Prophylactically, one of the most satisfying results of the use of lyophilic plasma was the elimination of the fear of dental extractions. Thus, a dose of 150 cc. of plasma given prior to extractions reduced the coagulation time to normal; following extractions, the sockets were packed with dry plasma. Almost complete rehabilitation of one patient with severe hemophilia was accomplished by the use of injections of 125 cc. plasma given weekly for three months.

A fascinating series of studies on a hereditary hemophilia-like disease in swine is reported by Muhrer, Hogan and Bogart.⁹⁹

THE SPLEEN

The spleen still remains an organ "full of mystery." Hints of its various functions may be obtained, however, by removing it or by studying it

in relation to various clinical conditions. Studies of splenectomized material by Singer, Miller and Dameshek¹⁰⁰ disclosed an intimate spleen-marrow relation, a definite influence of the spleen on the thickness of the red cells and a similar influence on blood destruction. Following splenectomy, the leukocyte and platelet counts almost always increase, indicating (with bone-marrow studies) that the spleen normally exerts an inhibitory effect on the bone-marrow production of these cells. Howell-Jolly bodies and nucleated red cells, especially in abnormal states, appear in the peripheral blood, suggesting an influence of that organ on denucleation of the red cells. The red-cell population becomes thinner, as evidenced not only by various measurements but by an increased hypotonic resistance and the presence of target cells. The red cells, in their various passages through the spleen, probably become thicker and thicker and thus more hypotonically fragile; with the spleen removed, this process is retarded and the target cell becomes evident. This was shown experimentally by Miller, Singer and Dameshek¹⁰¹ in dogs and guinea pigs. Cruz and Robschey-Robbins¹⁰² found that in splenectomized dogs made anemic by bleeding or by the injection of acetylphenylhydrazine, the number of normoblasts in the peripheral blood during the first phase of the regenerative period was four times greater than that in the nonsplenectomized animal. These findings were also suggestive of a spleen-marrow relation, the spleen appearing to have an effect on the maturation or delivery of the nucleated red cell. I¹⁰³ have discussed various facts and fancies relating to the spleen, including such concepts as "hypersplenism." Normal hypersplenism, which occurs when the spleen is enlarged for almost any cause — infection, congestion, cirrhosis of the liver or splenic vein thrombosis — usually results in leukopenia, thrombocytopenia and granulocytopenia, and often in anemia. Despite the low counts in peripheral blood, the bone marrow is hyperplastic; immediately following splenectomy, the leukocyte and platelet counts rise and remain elevated. These findings may indicate a hypernormal effect of the spleen on the marrow. Abnormal hypersplenism is present when for some unknown reason the spleen exerts an unusual effect on the marrow, with resultant hemolytic anemia or thrombocytopenic purpura. In the latter condition, despite the lack of platelets in the peripheral blood, the marrow is crowded with megakaryocytes, which, however, fail to produce platelets. Directly after splenectomy, the megakaryocytes show intense platelet production and the platelet count increases rapidly. If these interpretations of the relations of the spleen and the marrow are correct, they indicate the elab-

oration by the spleen of hormones that have effects on the centers of red-cell, white-cell and platelet production in the marrow. The evidence is as yet purely circumstantial and must await further investigation for complete proof.

Felty's syndrome has recently received increasing attention. This is a disorder in which marked rheumatoid arthritis, splenomegaly and leukopenia are simultaneously present. Lockie, Sanes and Vaughan¹⁰⁴ adhere to Felty's original concept that, owing to the chronic rheumatoid infection, the spleen becomes affected and the leukocyte count is lowered. The sternal marrow in their 2 cases showed slight myeloid hyperplasia, and the spleen chronic nonspecific splenitis. Steinberg¹⁰⁵ points out that the leukopenia and the secondary anemia characteristic of the syndrome are not due to bone-marrow depression, since sternal-marrow biopsies showed a hyperplastic marrow. As he states, it seemed plausible that the spleen may act as a barrier in not permitting the blood to receive these cells in sufficient quantities. Splenectomy was accordingly performed in 1 case with a marked and permanent effect in bringing the leukocyte count to normal. In a similar case seen by me, the patient's leukopenia and neutropenia were so marked that she was subject to numerous attacks of pyogenic infection. The leukocyte count averaged 1000, with approximately 10 per cent polymorphonuclear leukocytes. Splenectomy was performed with the idea of bringing the leukocyte count to normal, especially since the bone marrow was found to show extreme hyperplasia of the leukopoietic tissue. Following operation, the white-cell count returned to normal and further infections did not occur. The platelet count, which also had been somewhat depressed, rose to normal levels and the patient's menorrhagia was alleviated. The results in these cases are probably related to the very interesting concept of primary splenic neutropenia developed by Wiseman and Doan.¹⁰⁶ The essential condition in 5 cases was profound granulopenia, panhyperplasia of the marrow and splenomegaly and recovery after splenectomy. Varying degrees of combination of hemolytic anemia and thrombocytopenia purpura were encountered and also corrected by splenectomy. It was assumed that a single mechanism — hypersplenism — was responsible for the anemia, leukopenia and thrombocytopenia, since all elements were increased after splenectomy. Thus, one may group primary splenic neutropenia with hemolytic anemia and thrombocytopenic purpura; all of which may be due to abnormal hypersplenism, as stated above.

Until recently, most cases presenting splenomegaly were immediately called Banti's disease or splenic anemia. Whether any such condition as

postulated by Banti exists is greatly to be questioned. Cirrhosis of the liver, splenic-vein thrombosis or portal hypertension due to various causes may result in splenomegaly, anemia and leukopenia. Similarly, Gaucher's disease, Boeck's sarcoid of the spleen and Felty's syndrome, as noted above, may all result in anemia, leukopenia and thrombopenia that respond to splenectomy. Banti's disease and splenic anemia are best considered as "wastebasket" diagnoses reserved for those cases that have either been studied superficially or in which all other diseases have been excluded. In the last year or two, "agnogenic myeloid metaplasia," as introduced by Jackson, Parker, and Lemon,⁶⁷ has vied with Banti's disease as the diagnosis in many cases of splenomegaly. The contention inherent in this rather impressive sounding term is that the spleen may be the site, for no known cause (agnogenically), of active but ectopic bone marrow hyperplasia. That the spleen ever develops myeloid metaplasia independently, except in chronic myelogenous leukemia, is to be seriously questioned. Fibrosis, sclerosis or aplasia of the bone marrow, or its invasion by leukemia, lymphosarcoma, Gaucher's disease and so forth, may result in such extensive depletion of the normal bone marrow that various tissues attempt to take up the burden. This is customarily done by embryonically active hematopoietic organs such as the spleen and the liver, but such organs as the lungs and the adrenal glands may participate.

The end result of bone marrow displacement plus myeloid metaplasia in the spleen is often a blood picture characterized by normocytic anemia, leukocytosis with the presence of immature granulocytes, reticulocytosis and polychromatophilia, together with the presence of nucleated red cells. The blood picture (and the splenomegaly) may thus resemble chronic myelogenous leukemia, but the trephine bone marrow biopsy shows the true marrow condition, which is either that of fibrosis or of replacement by various abnormal cells. Polycythemia vera may terminate in a similar end picture frequently miscalled chronic myelogenous leukemia. Severe hemolytic anemia of the acquired type, particularly if it is of several months' duration, may also result in myeloid metaplasia of the spleen and liver. Jackson and his collaborators contend, however, that the metaplasia of the spleen may be inherent in that organ and that hemolytic jaundice, osteosclerosis, fibrosis of marrow and so forth, are simply accompanying rather than primary features. If this is the case, it would be indeed harmful, as these authors maintain, to remove the spleen or treat it by x-ray, since this organ is producing useful blood cells. Setting aside the matter of whether the splenic disorder is primary or not, it seems to me that a carefully done

sternal trephine bone marrow biopsy should help to settle this question. If the marrow is aplastic, fibrotic or invaded by foreign tissue, splenectomy should certainly not be performed; if, on the other hand, it is hyperplastic and the patient shows hemolytic anemia, removal of the spleen should be seriously considered. Reich and Rumsey¹⁰⁷ recommend biopsy of the spleen through the peritoneoscope in doubtful cases. They state that the presence of myeloid metaplasia definitely establishes the diagnosis of agnogenic myeloid metaplasia of the spleen. This is quite contrary to my views, as stated above, and also to some of Reich and Rumsey's own case reports. Thus in Case 2 when a bone marrow biopsy was finally done—after splenectomy—it showed fibrosis. In Case 3, there was slight jaundice and the red-cell count rose from 3,000,000 to 6,000,000 after splenectomy; this case might well have been one of hemolytic anemia. In Case 4, which showed myelocytes in the blood and an essentially normal marrow at puncture biopsy, the white cell count after splenectomy rose to 134,000 (!), which might well indicate that leukemia was present. Case 5, which presented a fairly typical picture of hemolytic anemia, was not splenectomized. At autopsy, the bone marrow was erythroblastic. Critical examination of these cases leads one to suspect that enthusiasm for a "new" syndrome may result first in calling many diverse types of cases examples of this condition, and secondly in withholding appropriate therapy like splenectomy, from certain others. That fibrosis of the marrow, particularly after polycythemia, occurs and is associated with a leukemoid blood picture and myeloid metaplasia of the spleen is quite certain. That the latter is ever primary is, however, questionable.

Primary neoplasms of the spleen are rare. I have recently seen a case of primary lymphosarcoma and one apparently of primary Hodgkin's disease of that organ. Pines and Rabinovitch¹⁰⁸ give a full report of a case of hemangioma of the spleen. An interesting neoplasm is that of hamartoma, as described by Sweet and Warren.¹⁰⁹ Here the spleen is the site of a neoplasm or neoplasms composed of new but normal splenic tissue.

The days when splenectomy was performed for almost any enlargement of the spleen have practically gone. Splenomegaly may be due to a large number of diverse conditions. In general, these are: infections (typhoid fever, malaria, syphilis, tuberculosis, Boeck's sarcoid and so forth); hyperplasias (leukemia, Hodgkin's disease, lymphoma and myeloid metaplasia); increased blood destruction (hemolytic anemias of various types); portal hypertension (cirrhosis of the liver and so forth); storage disorders (Gaucher's disease and so forth); and increased blood volume (polycythemia). Determination of the cause of the enlarged spleen in a

given case may be quite difficult, requiring careful and at times intricate studies of the blood, bone marrow and bones, the liver function, the serology, the esophagus (for varices) and so on. Puncture biopsy of the spleen, which is recommended by some workers as a harmless procedure and of considerable diagnostic value, should not be undertaken too lightly because of the danger of hemorrhage.

Splenectomy must be considered primarily from the physiologic standpoint and not from that of the degree of splenic enlargement. Some of the largest spleens are seen in cases of chronic myelogenous leukemia and polycythemia and in occasional cases of Hodgkin's disease; these are best left alone. Some of the smallest spleens may cause the greatest trouble, as in thrombocytopenic purpura and leukopenia.

Definite indications for splenectomy are severe fulminating thrombocytopenic purpura and severe acute or subacute hemolytic anemia. In both these conditions, it is presupposed that definite causes for the purpura and the hemolytic reaction have been ruled out. To procrastinate in either condition is to invite disaster, either from hemorrhage in the first instance, or from persistent hemolysis in the second. In mild cases of idiopathic thrombopenic purpura, splenectomy need not be seriously considered. There is a growing indication for splenectomy in severe leukopenia and granulocytopenia, provided various well-defined causes, such as leukemia (aleukemic), aplasia and Hodgkin's disease, can be ruled out by bone-marrow studies. As noted above, Felty's syndrome with marked leukopenia may be a perfectly good indication. This may also hold true in Boeck's sarcoid, Gaucher's disease and portal hypertension when one or several of the triad of thrombocytopenia, leukopenia and increased hemolysis are present to a marked degree. Whether the spleen should be removed routinely in cases of portal hypertension, particularly when the liver is thought to be normal (splenic-vein thrombosis and Banti's disease), is debatable. In an excellent article on the present status of surgery of the spleen, Pemberton¹¹⁰ states that splenectomy in Banti's syndrome "lightens the load that has been thrown on the liver by reducing the volume of blood entering the portal circulation, removes possible toxic substances originating in the spleen, removes the splenic factor in blood destruction and produces adhesions for the establishment of collateral circulation." ¹¹¹ I cannot, so optimistic, it must be admitted that: probably some justification for these studies. The end-results of a ten-year follow-up of a sufficient number of splenectomized patients, hyp

without hematemesis, are not yet at hand. Pending this, the ultimate value of splenectomy in this group of cases must be kept *sub judice*. Occasionally, the spleen should come out because its large bulk in a child actually interferes with locomotion and therefore with further physical development. I have had this done in cases of Gaucher's disease, Cooley's anemia and sickle-cell anemia, with results that have been, at least temporarily, excellent.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29061

PRESENTATION OF CASE

A forty-eight-year-old Polish garment worker entered the hospital because of abdominal pain and weight loss.

Four months before entry the patient developed a rather vague upper abdominal pain, which was most marked on pressure over a point midway between the xiphoid and umbilicus. The pain was usually relieved by drinking milk and aggravated after eating meat. The patient occasionally felt nauseated but seldom vomited. Laxatives at first relieved the pain, but after a few weeks even these proved ineffective. He also noted swelling of the abdomen and ankles, the latter being present in the morning as well as the evening. Three months before entry he was seen in the Out Patient Department, where physical examination revealed a somewhat distended but nontender abdomen. The liver edge was palpable on deep inspiration, and the upper level of liver dullness was percussed to the fourth interspace. The spleen was not felt. Normal peristaltic sounds were audible. There was questionable bilateral ankle edema. Examination of the blood was not remarkable, and both a barium meal and a barium enema were negative. A chest roentgenogram showed a high diaphragm on both sides, with linear areas of atelectasis in the lungs. The heart was transverse in position and not enlarged. The aorta was remarkably tortuous but showed no actual widening. During the next three months, despite extensive study, no diagnosis was established. On one examination shifting dullness in the abdomen was found. A bromsulphalein test showed 5 per cent retention of the dye in the serum. During the period of illness he lost 20 pounds. He denied diarrhea, tarry, bloody or acholic stools, dysuria, pyuria and hematuria. He had suffered with nocturia (two times) for several years. Because of the persistence of symptoms and the lack of a diagnosis, hospital admission was advised.

The family history was noncontributory. The past history was not remarkable, except that the patient had always consumed large amounts of wine and beer.

Physical examination on admission revealed a well-developed man who did not appear to be in great distress. He had obviously lost a great deal of weight. The edges of the tongue were smooth and somewhat redder than normal. Examination of the heart and lungs was normal. The abdomen was full, particularly in the right lower quadrant, where no mass could be felt but percussion demonstrated a localized area of flatness. In the upper abdomen, the rectus muscles were separated in the midline for a distance of 4 cm. There was tenderness in the left calf on palpation and on movement of the left ankle. The left leg was 32 cm. in circumference at the calf and the right 31 cm. The left foot seemed warmer than the right and the pulsation of the dorsalis pedis artery was stronger on the right than on the left.

The blood pressure was 165 systolic, 102 diastolic. The temperature was 98.6°F., the pulse 92, and the respirations 15. The temperature ranged between 97 and 101°F. and the pulse between 70 and 120 on the four succeeding days.

Examination of the blood revealed a hemoglobin of 74 per cent, a red-cell count of 4,500,000 and a white-cell count of 10,300, with 64 per cent polymorphonuclear leukocytes. The urine was normal. The stool was guaiac negative on three examinations. The blood Hinton test was negative, and another gastrointestinal x-ray series was negative.

A peritoneoscopy was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. CHESTER M. JONES: "Four months before entry the patient developed a rather vague upper abdominal pain, which was most marked on pressure over a point midway between the xiphoid and umbilicus." I suppose they mean tenderness that was increased by pressure rather than pain that the patient felt.

The physical examination apparently confirms the patient's statement that there was pain on pressure in the midabdomen. The examination also seems to indicate that the liver really was enlarged.

The high diaphragm by x-ray might have been due to the large liver or to abdominal distention. The linear areas of atelectasis probably meant old pulmonary infarcts.

"The patient had always consumed large amounts of wine and beer." I suppose that is an attempt to sell me a diagnosis.

According to the record it seems clear that what was at first believed that this patient had cirrhosis of the liver. But as the story develops there are many discrepancies so far as such a diagnosis is concerned. I am sure that I am not going to

able to give a diagnosis that will be any more than tentative, but there are certain facts I should like to point out.

There is no mention of rectal examination but something was felt in the right lower quadrant. Was a rectal examination done on this patient?

DR. TRACY B. MALLORY: Yes. The right lobe of the prostate felt harder than normal but seemed to be normal in size.

DR. JONES: Would you trust a statement of that sort, Dr. Colby?

DR. FLETCHER H. COLBY: Not entirely.

DR. JONES: Neither should I. One should state that rectal examination showed an asymmetrical prostate, the right lobe being harder than normal. Another point should be made—namely, that no rectal mass was felt outside the prostate; that is important.

So far as the x-ray films are concerned, the heart is transverse, and I shall pay no attention to it. There seems to be a suggestion of displacement of the small bowel from the right lower abdominal quadrant. Certainly the x-ray findings are not distinct nor do they appear to be helpful. One thing can be said: there is no evidence of intrinsic gastrointestinal disease. It is also important, if we have the right to make the statement, that no esophageal varices were demonstrated. I assume that, with two gastrointestinal series, varices were looked for and apparently not demonstrated. This is an oblique film, and I should not say that the stomach or duodenum is displaced, nor is the duodenal curve. At least there is lack of evidence of an extrinsic pressure defect around the stomach or duodenum. This is a good picture of the jejunum without any evidence of disease.

The story is short—apparently four months—and is entirely consistent with a new growth, either primary or secondary to what had hitherto been a silent cirrhosis. He had a tremendous loss of weight,—20 pounds in four months,—without much vomiting. To be sure it was probably due to a lack of food intake; but it occurred. The patient had a mass with vague gastrointestinal symptoms. There is nothing in the record that gives any clue concerning the nature of the pain. It is poorly described. One can say that neoplasm should be seriously considered. We are hard pressed to believe that it was ulcer pain. It was not relieved by the things that relieve ulcer—milk, soda and so forth. The statement that meat made the pain worse is curious.

DR. MALLORY: He evidently gave a confusing story, Dr. Jones. The record says, "A very confusing story but the point which on reiteration seems definite is that the present illness came on within the past year and consisted of a constant

aching pain just above the umbilicus that was worse after eating a heavy meal and not definitely relieved by milk."

DR. JONES: One can say that it is an atypical story. There is nothing characteristic about it, and this fact is against the diagnosis of peptic ulcer. There are no cardiorespiratory symptoms, a point worth something in excluding certain diagnoses. Another fact that should be pointed out is that for two years he had had nocturia, never having previously noted it. I gather there was more or less language difficulty and that it was impossible to get an accurate story.

On physical examination the patient was emaciated and showed definite evidence of deficiency disease, which was probably secondary rather than the cause of the symptoms. It was evidenced by a loss of weight, a smooth red tongue, and, possibly, the appearance of edema from time to time. The liver on examination was palpable on inspiration, and the upper edge was at the fourth interspace or fifth rib. The diaphragm was certainly high, and it is quite possible that this patient really had a big liver, but at the time of physical examination on admission to the hospital absolutely nothing is said about the liver so one has the right to be skeptical about the enlargement noted in the Out Patient Department. I am not at all sure the liver was enlarged. If it was, then it subsequently diminished in size. The spleen was not palpable at any time. There is a definite note made to that effect. From these films, so far as I can tell, it seems fair to say that the spleen is not enlarged. If this patient had cirrhosis of the liver, which I doubt, with the edema and ascites that are supposed to have been noted one should expect to have been able to demonstrate some enlargement of the spleen.

On admission there were other physical findings that may be of importance—namely, signs of thrombophlebitis in the left leg, with an area of tenderness, increased warmth and possibly some edema. There was evidence of tortuosity of the aorta and of arteriosclerosis. But I think these two factors do not need to interest us too much. There was no anemia of importance. At least on one examination the lungs and heart were normal. The urine and stools were normal, and a Hinton test was negative. The bromsulfalein test showed 5 per cent retention at the end of half an hour. In other words, the laboratory findings are not diagnostic or helpful. All the x-ray studies were reported to be negative and serve only to exclude disease rather than to make a diagnosis. Fever was present, without leukocytosis. If this patient had a thrombophlebitis it is possible that the elevation of temperature to 101°F. may have been

due to a local inflammatory process in the leg. It is curious that there was no leukocytosis. I am inclined to think that the fever was due in part to what was going on in the leg. If there was intrahepatic disease, that fact, regardless of the nature of the disease, would lead us to expect slight elevation in temperature from time to time.

With these facts, or near facts, and negative findings, how can one make a diagnosis? I do not believe it is possible. The important thing to do is to arrive at the decision of what to do, having excluded certain things. Cancer of the gastrointestinal tract seems unlikely. It is possible to have a small lesion of the colon, miss it on the x-ray films and have the liver full of metastases. We have seen such cases. However, there is no evidence that this is the case here. The stool was negative, and there was no evidence of occult bleeding. Everything is against gastrointestinal cancer. Again, so far as one can tell there is no evidence of pancreatic enlargement. A cancer of the pancreas, clinically, is unlikely, and I think it was not present.

Did this patient have cirrhosis of the liver? He had an alcoholic history and a palpable liver on one occasion, he was said to have had shifting dullness in the abdomen, and he had edema on a few occasions in the legs. If that story is true one must entertain the diagnosis of cirrhosis of the liver. One fact in favor of it is the indefinite gastrointestinal story, but against it are the demonstration of an enlarged liver at the second examination, the failure to demonstrate the spleen or esophageal varices and the absence of retention of dye. If edema and ascites are associated with cirrhosis, one would expect to get a more specific set of findings than are available here. Furthermore, there was no anemia, and usually the patient with cirrhosis that comes into the hospital is moderately anemic. Therefore, I think that the logical diagnosis is not that of cirrhosis. We have seen many cirrhotic patients in this hospital whose symptoms are not due to the lesions of the liver; such a cirrhosis in a sense may be called compensated and not the dominant part of the history. The cirrhosis here, if it was cirrhosis, was not the cause of the symptoms. If that is true, how can we explain them on the basis of the findings we have? I confess I cannot do it. The best I can do is to suggest that he had a malignant tumor that had not been located. There is one curious statement—namely, that there was no mass in the right lower quadrant but flatness and, I take it, an increased sense of resistance. That is the most that they could say on physical examination. We do know that he had signs of thrombophlebitis in the left leg. I believe that this patient had a malignant tumor.

It may have been retroperitoneal or lower abdominal, and there may have been metastases in the liver. I am sure the decision to explore this case by means of peritoneoscopy was advisable. If cirrhosis was found and nothing else, I do not understand the symptoms.

DR. MALLORY: You see no contraindication to the use of the peritoneoscope in this case, Dr. Jones?

DR. JONES: I think peritoneoscopy should be done. However, the incision should be made as high as possible above the umbilicus because there is the suggestion that something is not right in the lower abdomen and therefore one should keep as far away from this area as possible. My idea in examining this patient would be that one should try to establish two things: first, the presence or absence of liver disease and, second, to see what else there was in the peritoneal cavity. The risk of peritoneoscopy as I see it is minimal and one that has to be accepted to gain further information.

DR. EDWARD B. BENEDICT: Peritoneoscopy showed the abdomen to be so full of adhesions that no air space could be obtained. No implants or tubercles were seen on the adhesions. I could not examine the peritoneal cavity. I tried in two places, just above the umbilicus and then below, and encountered adhesions in both places.

CLINICAL DIAGNOSIS

Carcinoma of liver or peritoneum?

DR. JONES'S DIAGNOSIS

Malignant tumor (abdominal or retroperitoneal).

ANATOMICAL DIAGNOSIS

Tuberculous peritonitis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Although Dr. Benedict wisely desisted when he encountered adhesions, twenty-four hours following the peritoneoscopy it became obvious that fecal material was draining from the peritoneoscope wound. The patient was therefore taken to the operating room and explored. A generalized adhesive peritonitis was found, and biopsy of the omentum showed that it was tuberculous in nature. An effort was made to seal the point of perforation, which to date has been unsuccessful. The patient still has a draining fistula.

DR. JONES: Was there free fluid in the peritoneal cavity?

DR. MALLORY: No. Is it correct, Dr. Benedict, that we have had other cases of tuberculous peritonitis in which peritoneoscopy has been either difficult or impossible?

CASE 29062

PRESENTATION OF CASE

DR. BENEDICT: There was one in which I perforated the colon but recognized it right away. The patient was explored immediately, and the opening sutured. But in this case there was no fecal odor, and I know that I was not actually in the bowel. I knew the diagnosis as soon as I found so many adhesions; at least I was reasonably sure that it was tuberculous peritonitis.

DR. MALLORY: The one other type of case that would be equally dangerous would be a diffuse carcinomatous process with adhesions.

DR. BENEDICT: They never give any trouble. I have had a lot of those cases and have never encountered the firm adhesions that you do in tuberculous peritonitis.

DR. MALLORY: So I take it, that if you thought there was a real likelihood of tuberculous peritonitis you would not attempt peritoneoscopy.

DR. BENEDICT: Not if it was the adhesive type.

DR. JONES: I think it is interesting that the x-ray films apparently showed no distortion of the silhouette of the bowel anywhere, or displacement.

DR. MALLORY: After he knew the diagnosis, Dr. Schatzki reviewed the films taken at the time of the small-bowel enema and made this comment:

Restudy of the films of the small-bowel enema, after being informed about the findings at operation, show that more attention should, perhaps, have been paid several factors. The small intestines filled particularly easily. The loops of the small intestine were grouped in a somewhat too regular order and the tract was, perhaps, slightly shortened. The lower border of the small intestine appeared somewhat smoother and somewhat higher than that usually seen. No intrinsic lesion, however, was present. All these findings together should have made one wonder whether these findings were not consistent with an intraperitoneal chronic disease such as tuberculous peritonitis.

But even after knowing the diagnosis, he did not think that there was anything definite. He believes he might have suspected it.

DR. JONES: I should think one could explain the edema on the basis of malnutrition—that is, nutritional edema. Whether there was ascites at the time it was thought to be present is questionable.

DR. MALLORY: A few months before entry ascites may well have been present. At the time of operation, the peritonitis was the dry adhesive type.

A fourteen-year-old girl was admitted to the hospital because of severe abdominal pain.

Two weeks prior to admission, while at camp, the patient suffered with sharp pain in the left lower quadrant, which disappeared spontaneously after two days, without medical care. Approximately four and a half hours prior to admission she was suddenly seized with a similar, but severer, acute, knifelike, intermittent pain in the left lower quadrant involving a 5-cm. area just above and parallel to Poupart's ligament. A short time later the pain radiated to an area above the symphysis pubis. Her physician apparently administered morphine with only slight relief. At times there was a "heavy sensation" in both labia, and slight pain along the medial aspect of the left thigh. There was moderate urgency initially, but this disappeared. The patient had no chills but felt feverish. There was no nausea, vomiting, diarrhea, distention, bloody or cloudy urine or other urinary symptoms.

The family history was noncontributory. The patient was said to have been kicked in the left groin three years previously but suffered only local tenderness, which subsided within a few days. Three months later she was said to have had "catarrhal jaundice," which lasted two weeks. She denied sexual intercourse. Her menses had been normal except that one week before periods there was a slight amount of thick white discharge. The last menstrual period had occurred nineteen days before the present illness. Her cycle was twenty-eight days, and the menses lasted five days.

Physical examination disclosed a well-developed and well-nourished girl who held her left side and cried because of the pain. Examination of the heart and lungs was negative. There was only mild tenderness and spasm in the left lower quadrant, and apparently costovertebral-angle tenderness was not elicited. No masses were felt. There was a slight mucoid vaginal discharge. The inguina admitted two fingers. The cervix was firm and freely movable without associated pain. There was an oblong exquisitely tender mass in the posterior cul-de-sac, which seemed to be a part of the retroverted uterus. It was firm, smooth, movable and about the size of an orange, with a round superior pole that extended up to the left lower quadrant. The ovaries were not felt. Rectal ex-

amination did not contribute any further information.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 100.4°F., the pulse 76, and the respirations 20.

Examination of the blood revealed a white-cell count of 20,500. The urine was normal. A stool was guaiac negative. A cervical smear was negative for gonococcus. A flat plate of the abdomen revealed no unusual soft-tissue masses or areas of calcification.

An operation was performed several hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. GORDON DONALDSON: In this case I am afraid the x-ray films are not going to be of much help. I had hoped that the soft-tissue mass might at least be seen, and that we might even be able to see some radio-opaque areas within it. Perhaps Dr. Schulz can outline the mass.

DR. MILFORD D. SCHULZ: Any soft-tissue mass that may be here is indefinite. It would be "sticking one's neck out" to say that such a mass is present.

DR. DONALDSON: With the history of trauma to the left lower quadrant three years previously and with the pain running down along Poupart's ligament with inguinal distribution, I think we must at least mention the possibility of weakness of the abdominal wall or even an actual herniation. However, there was nothing on physical examination to support this suggestion. The urinary tract, too, with this type of radiation might be mentioned as the cause of this girl's pain. A badly prolapsed kidney in the region of this mass would, I should think, have been either atrophic or hydronephrotic by this time and there would have been some urinary findings, which we do not have. The only urinary symptom, moreover, was urgency. I shall also eliminate the gastrointestinal tract, since there was nothing in the history or physical examination to suggest such a lesion.

There is no note in the record of just when her catamenial life began, but I should guess that she had been having periods for a year and a half or two years. This is an ideal time for a hematosalpinx, but to have a large amount of blood in one tube, with the remainder of the genital tract functioning normally and with an undisturbed menstrual cycle, is most unusual.

A tumor of the uterus itself, such as a fibroid, should be mentioned as a possibility. In a young girl who had been menstruating for only a year and a half a fibroid of these dimensions is unlikely.

A tubo-ovarian inflammatory mass should also be considered, particularly since the mass was exquisitely tender. The patient did have a white-cell count that would go with an abscess in that location and she also had a vaginal discharge which was suggestive enough to make someone do a smear. However, there are some inconsistencies with this diagnosis: she was not sick enough, and the temperature and pulse were out of proportion to the white-cell count.

That brings us down to an ovarian tumor, such as a cyst, a fibroma or a dermoid. A tumor of the ovary that had twisted on its pedicle, thus cutting off its blood supply, is an adequate explanation for the elevated white-cell count, the degree of pain and the site of radiation of the pain, although one might have expected that the patient would also have had back pain. The local pressure that such a tumor would exert on the bladder accounts for the urgency and also for the mucoid vaginal discharge. This was probably a dermoid, inasmuch as dermoid is the most prevalent ovarian tumor in a girl of this age; however, I shall not go that far and shall just say that it was an ovarian tumor.

CLINICAL DIAGNOSIS

Twisted ovarian cyst.

DR. DONALDSON'S DIAGNOSIS

Ovarian tumor with twisted pedicle (? dermoid).

ANATOMICAL DIAGNOSIS

Twisted ovarian cyst.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The operation showed that this girl did have a cyst of the ovary. The ovary and tube had twisted on themselves four times, completely infarcting both organs. They were not adherent to surrounding structures, however. The cyst apparently was a simple one, since it contained clear serous fluid. It was not a dermoid. The infarction had completely destroyed its lining cells so that a more exact definition of its character is impossible.

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EPIDEMIC KERATOCONJUNCTIVITIS

An epidemic of keratoconjunctivitis occurred among shipyard workers on the Pacific Coast in 1941.* Since then the disease has gradually spread eastward and has finally appeared in various cities on the eastern seaboard. From an economic standpoint it is of considerable importance, since it disables the worker from two to eight weeks and may seriously interfere with production in any plant where an epidemic takes place.

The etiologic agent is thought to be a virus, particularly since no pathogenic organisms have been

recovered from the conjunctival secretions. Scrapings from the conjunctiva show a preponderance of mononuclear cells. The incubation period is from seven to twelve days.

Symptoms consist of a foreign-body sensation in the eye, lacrimation, photophobia, swelling of the lids and enlargement of the preauricular and, sometimes, the submaxillary lymph nodes. There may be slight fever and general malaise. In the early stages the eye shows marked edema of the conjunctiva and the lids. The eye is watery, but there is little or no purulent discharge. After five to ten days there is an involvement of the cornea in from 40 to 60 per cent of the cases. This consists of small subepithelial infiltrates chiefly confined to the central zone of the cornea. The conjunctival symptoms usually subside in from one to three weeks, but the keratitis may remain active for many weeks. As a rule the disease runs a regular course that is little, if at all, influenced by any form of treatment. Since no specific therapy has been worked out, it is better to treat conservatively rather than overzealously. Cold compresses and mild soothing lotions and ointments afford relief, and atropine is indicated if the cornea becomes affected.

Transmission is by direct contact, contaminated hands, instruments, eyedroppers, towels and so forth, and the disease is communicable so long as the conjunctivitis is active. Affected patients should be isolated and should be carefully instructed in eye hygiene. Scrupulous care should be exercised by the physician and his attendants to avoid transfer of the infectious agent: the hands should be washed after examining affected eyes, and instruments and eyedroppers should be sterilized. Although not officially listed as a reportable disease, all suspected cases should be immediately reported to the Division of Communicable Diseases, Massachusetts Department of Public Health, to the Division of Occupational Hygiene, Massachusetts Department of Labor and Industries or to the Division of Industrial Safety, as is brought out in a letter published elsewhere in this issue of the *Journal*.

*Hogan M J and Crawford J W. Epidemic keratoconjunctivitis. *Am J Med* 1942; 2: 984-994.

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MEDICAL EPONYM

STELLWAG'S SIGN

"Ueber gewisse Innervationsstörungen bei der Basedow'schen Krankheit [Certain Disturbances of Innervation in Basedow's Disease]" were discussed by Professor Carl Stellwag von Carion (1823-1904), of Vienna, in an article which appeared in the *Vienna Medizinische Jahrbucher* (17: 25-54, 1869). A portion of the translation of his remarks after presenting his theory concerning the disturbances of innervation follows:

This peculiar pathologic relation is not simply an unrelated, curious finding, but occurs repeatedly in the disturbances of motility of the lids which are a constant feature in Basedow's disease. Examples are the abnormal wideness of the palpebral fissure, infrequency and incompleteness of involuntary closure of the lids, and failure of the upper eyelid to participate when the plane of direction of the eyes is elevated or lowered. . . . I have not found this second peculiar phenomenon (*infrequency and incompleteness of involuntary closure of the lids*) explicitly mentioned anywhere in the literature; yet in my observation, it is among the most constant and, indeed, characteristic eye symptoms of Basedow's disease.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

ANALYSIS OF CAUSES OF MATERNAL
DEATH IN MASSACHUSETTS DURING 1941MISCELLANEOUS (*Concluded*)

During 1941, one death was due to poisoning from diethyl stilbestrol and sulfadiazine. This patient had diabetes. During her pregnancy she had had pyelitis, for which she had been given sulfadiazine; she was also given rather large doses of diethyl stilbestrol. Following her delivery, which was by cesarean section, she had an uncomplicated convalescence until she returned home. Recurrence of the pyelitis was treated by sulfadiazine. Persistent jaundice developed, which resulted in death. Autopsy showed a toxic hepatitis, acute pyelitis and acute nephritis with focal necrosis. This was a tragic disaster.

There was one death due to aneurysm. This patient had had one previous delivery. Her pregnancy had been uneventful until the onset of the fatal illness. The record does not state how far the pregnancy had advanced, but it is reasonable to infer that it was beyond seven months because cesarean section was performed

subsequent to laparotomy. The present illness developed suddenly while the patient was mopping the floor. She was said to have had a severe pain in the abdomen and collapsed. She was seen within half an hour and was immediately transferred to a hospital. On entry, the systolic blood pressure was 60, and the pulse 120 and of poor quality. Since the patient presented a picture of extreme shock, immediate laparotomy was decided on. The peritoneal cavity was full of blood, but no definite cause for hemorrhage was found; a cesarean section was performed, there being no statement concerning the condition of the infant. Death occurred twelve hours after operation. An autopsy showed a spontaneous rupture of an aneurysm of the splenic artery. This case illustrates the extreme value of post-mortem examination, without which no specific diagnosis could have been made.

One death was due to hydatidiform mole. This patient was a primipara who was first seen when approximately twelve weeks pregnant, because of bleeding. She was seen in consultation and kept in the hospital 12 days. The diagnosis of threatened miscarriage was made. The bleeding was scanty, and at the end of 12 days the patient was allowed to go home. Three weeks later she began to bleed profusely during the night and was sent to the hospital. On arrival, the pulse was 100. Two hours later a vaginal examination revealed grapelike masses in the vagina. The uterus was curetted, and the vagina was packed. Bleeding was excessive, and the patient died on the operating table. Had a correct diagnosis been made during the patient's first hospital stay and had the uterus been emptied at that time, it is likely that a fatal hemorrhage would not have occurred.

One patient died of psychosis. She was a primipara who was delivered by a cesarean section because of "cervical stenosis." She had lost 20 pounds in the last eight weeks of pregnancy. Following delivery the patient developed a psychosis and would not eat. The psychosis was manic in type, and death resulted from exhaustion and terminal bronchopneumonia, secondary to the psychosis.

One death was due to anaphylaxis. This patient had had eight previous deliveries, all the children being alive and well. She was known to have bronchial asthma, with a particular sensitivity to aspirin. She was delivered normally, and left the hospital seven days later. Two weeks after she had returned home she developed a cold and took some "special cold tablets." An asthmatic attack developed immediately and while being

sent to the hospital in a taxicab, the patient died. This was not a true obstetric death, but since it occurred during the puerperium, it must be so classified.

One patient died of cancer. This patient had three living children. In the fourth pregnancy she was sent to the hospital between the sixth and seventh months, complaining of tenderness in the right lumbar region. There had apparently been no prenatal care. A consultant found a mass in the left breast. At operation on the following day, a scirrhus cancer of the breast was found and the breast was removed. The patient died on the eighth postoperative day; the cause of death was listed as "carcinoma of the breast with carcinomatosis."

Five nonobstetric deaths that were reviewed have not been analyzed.

DEATH

COOK — WILLIAM W. COOK, M.D., of Quincy, died January 23. He was in his fifty-seventh year.

Born in Newcastle, Maine, Dr. Cook received his medical degree from Tufts College Medical School in 1910. He practiced in the Panama Canal Zone for ten years and then in Maracaibo, Venezuela. He was a member of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons.

His widow, three daughters, a son, a brother and a sister survive him.

CORRESPONDENCE

EPIDEMIC KERATOCONJUNCTIVITIS

To the Editor: A severe and highly contagious form of conjunctivitis, which has been given the name "epidemic keratoconjunctivitis," appeared among shipyard workers in California in September, 1941, and has already appeared in epidemic form in New England. Many doctors have undoubtedly never seen and possibly have never heard of this condition. There are sufficient data to indicate that the disease may easily be transmitted to uninfected persons under treatment for relatively trivial diseases or injuries to the eyes. Three of the four major outbreaks of this disease have occurred in large industrial groups.

The enclosed outline is being sent to physicians and others concerned, to give a clear idea of what to guard against, so that a serious outbreak of a disease which could interfere materially with our total war effort may be prevented.

PAUL J. JAKMAUH, Commissioner of Public Health

JAMES T. MORIARTY, Commissioner of Labor
and Industries

A. WILLIAM REGGIO, Surgeon (R), U.S.P.H.S.
Director, Medical Division,
Massachusetts Committee on Public Safety

GEORGE L. SCHADT, President,
Massachusetts Medical Society

EPIDEMIC KERATOCONJUNCTIVITIS

Causative Agent. Presumably a virus.

Incubation Period. Seven to twelve days.

Means of Transmission:

- (1) Direct contact.
- (2) Contaminated hands, instruments or towels.

Diagnosis:

- (1) Edema of one or both lids.
- (2) Moderately profuse lacrimation.
- (3) Acute follicular conjunctivitis (palpebral and bulbar conjunctivas are both involved).
- (4) Early lymph-node involvement, usually with swelling and tenderness of preauricular nodes.
- (5) Negative culture.
- (6) Development of pseudomembrane in conjunctival sac.
- (7) Smear of conjunctival scrapings shows mixed response, with predominance of mononuclear cells.
- (8) Development of corneal opacities (a late, not an early, development).
- (9) Opacities are small grayish areas below the epithelium, probably located in Bowman's membrane.

Course. In the early stages of the disease, diagnosis is difficult, and the early development of enlargement of the preauricular node should be watched for. The conjunctivitis usually persists ten days or longer, and the corneal opacities generally appear about as the conjunctivitis seems to be disappearing. The usual therapeutic agents are of little or no use, and no specific therapy is yet available. About 50 per cent of the cases develop bilateral involvement. The disease has been known to persist as long as eight weeks. In one epidemic, 85 per cent of the patients developed corneal opacities, and these appear to be permanent in the majority of cases.

Treatment. There is no specific therapy. Sulfonamide ointments and solutions have been used extensively. Cold compresses seem to produce more relief from discomfort than hot.

Recommendations:

- (1) Meticulous cleansing of hands and instruments by physicians, nurses and so forth.
- (2) Use individual eyedroppers.
- (3) Establish early diagnosis.
- (4) Isolation of infected patients.
- (5) Education of patients in measures of general cleanliness and eye hygiene.

Outbreaks of this disease, real or suspected, should be reported immediately to one of the three following agencies, from which further information may be obtained:

Division of Communicable Diseases
Department of Public Health

519 State House, Boston (CAP 4600)

Division of Occupational Hygiene
Department of Labor and Industries

23 Joy Street, Boston (CAP 0687)

Division of Industrial Safety
473 State House, Boston (CAP 4600)

Research in the epidemiologic and bacteriologic aspects of the disease is being carried on under the direction of Dr. Murray Sanders, Columbia University College of Physicians and Surgeons, 630 West 168th Street, New York City.

HAND-SCHÜLLER-CHRISTIAN DISEASE

To the Editor I regretted to see in the November 12 issue of the *Journal*, which I peruse regularly, that the eponym for the week [Schüller-Christian] left out the name Hand' from the condition that he was the first to describe. In fact I have always thought that Schüller added less than either Henry Christian or Dr Hand (who, by the way, is still practicing in Philadelphia) although together they did not give an adequate nosologic picture. Certainly Hand's description appeals to me as nearer the mark than Schüller's conclusions that are translated

E B KRUMHAAAR MD

The School of Medicine
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Philadelphia

* * *

Dr Krumhaar's letter was referred to Dr Robert W. Buck, the author of the eponyms; his reply was as follows:

To the Editor I read with interest Dr Krumhaar's letter concerning Hand-Schüller-Christian disease. My original typescript regarding Schüller-Christian disease must have been written nearly ten years ago, at which time I knew nothing of the xanthomatosis. As Dr Krumhaar points out, Hand was as nearly correct as either Schüller or Christian. I think the proper eponym at the present time is 'Hand-Schüller-Christian, and I should include the descriptions of all three authors.

ROBERT W BUCK MD

5 Bay State Road
Boston

REPORT OF MEETING

HARVEY SOCIETY

At a regular meeting of the Harvey Society of Tufts College Medical School, held at the Beth Israel Hospital on October 23, Dr Harold W. Brown, dean of the School of Public Health of the University of North Carolina, spoke on the subject 'Intestinal Anthelmintics'. Formerly, the treatment of helminthiasis was based on erroneous reasoning, being aimed at disgusting the parasites with foul smelling, foul tasting medicines. Fortunately for the far flung armed forces of the United Nations in the present world conflict, who are stationed in areas infested with these parasites, knowledge is now based on scientific facts; however, it is still incomplete so that some methods of treatment are empirical.

The chief characteristics of the group of worms that infest the intestinal tract are as follows: they usually have a digestive tract, most of them have a low grade nervous system, they have no heart, there is a rudimentary excretory system and they have a horny outer layer of chitin that is like the substance forming a fingernail. It becomes obvious, therefore, that anything which affects such an organism must also be toxic to some extent on the host. Furthermore, these intestinal helminths vary in habits, anatomy, size and position, so that shotgun therapy is of no avail. For example the hookworm is small and cannot be affected until the bowel is cleaned, whereas the ascaris is large and is not easily protected by food. This is one of the reasons for the rationale of purges. Further reasons for the employment of purges are to rid

the host of toxins and to wash out worms that may only have been stunned by the anthelmintic.

Anyone concerned with the therapy of helminthiasis should be able first to diagnose the kind of worm responsible. This requires a fundamental knowledge of the various kinds of eggs.

The hookworm is a parasite about 1.0 cm long that has teeth which fasten onto the wall of the intestinal tract of the host, therefore the aim of treatment is to break this grip. Chloroform was once used, this drug does stun the worm, but it is liable to injure the liver of the host. One part of chloroform is soluble in 200 parts of water; hence much is probably absorbed from the intestinal tract. In an effort to find a solution of lower solubility and toxicity, carbon tetrachloride was employed. Since 1 part of this is soluble only in 2000 parts of water, there is less absorption from the intestinal tract of the host. A subsequent purge rids the alimentary tract of the stunned worms and further decreases the chance of toxic effects. However, this drug was found to have fatal results once in 30,000 to 50,000 cases, and even such a low mortality cannot be countenanced in public health work where the good will of the community is needed. This led to further research and to the discovery of the efficacy and nontoxicity of tetrachlorethylene. Since the solubility of this drug is only 1 part in 12,000, intestinal absorption is practically negligible. Furthermore, this compound is available and relatively cheap. The dose is 3 cc. Giddiness is an occasional complaint and rare cases of coma occur. Alcohol increases the rate of absorption and therefore adds to the danger of toxic reactions.

Although carbon tetrachloride has been supplanted in the treatment of hookworm disease, it is still the treatment of choice in tapeworm infestation. Injury to the liver apparently occurs only in the presence of low calcium and carbohydrate reserves. In suspected cases of deficiency, therefore the patient should be given a high milk high-carbohydrate diet for some time before the anthelmintic is employed. These parasites grow from the head and therapy is aimed at this part of the organism. The weight of the rest of the worm which often is 15 to 70 feet long aids in freeing the head by gravity, even if the worm is only stunned. If the body and not the head is obtained there is no advantage in attempting treatment again for about two months, since it is rare that the head can be dislodged without the beneficial effect of the weight of the body.

A combined infestation with round worms (*Ascaris*) and hookworms is not infrequent, and its management entails some difficulties. Both carbon tetrachloride and tetrachlorethylene stimulate the former, and in an attempt to escape, they are liable to enter the biliary tract or peritoneal cavity. Careful diagnosis obviates this danger. Oil of chenopodium, of which ascaridole is the active principle, is effective against this worm, but is of relatively high toxicity, death occurring about once in every 20,000 to 40,000 cases. There is often a question of idiosyncrasy to the drug. Experiments were carried out with the phenol and resorcinol derivatives in an attempt to find a compound that would be effective and at the same time nontoxic. Increasing the side chain decreased the toxicity to both worms and man and it was found that the most potent anthelmintic for this species that was relatively safe for man was hexylresorcinol. This kills 95 per cent of the worms and cures 90 per cent of patients. The dose is 1 gm. This drug precipitates protein and

forms a close bond with it, so food should not be given for five hours before or after treatment. Because of this property of protein precipitation, hexylresorcinol may affect the mucous membrane of the buccal cavity if taken by mouth in its native state. Gelatin capsules are usually used, but these are difficult for children to swallow.

Whip-worm (*Trichuris*) is not effectively combated by any single drug, although any of the usual anthelmintics kill a few. *Leche de higuero* (milk of the fig tree) is said to have been used successfully in Venezuela, but this is a particularly foul-tasting substance, of which a dose of 60 cc. is required. Its action is supposed to be due to fecin, a specific enzyme, which kills the worm by digestion. This enzyme has not been isolated.

BOOK REVIEWS

Principles of Extraperitoneal Caesarean Section. By James V. Ricci, M.D. 8°, cloth, 224 pp., with 47 illustrations. Philadelphia: The Blakiston Company, 1942. \$4.50.

This monograph, divided into eleven chapters, deals exclusively with the various modalities of the lower-segment cesarean sections.

In the first chapter, entitled "Gastro-Elytrotomy," the authors discuss the principles of extraperitoneal cesarean section and show, by an extensive review of literature, the various steps in the evolution of this operation. In the second chapter, which covers the period from 1906 to 1940, the intra-abdominal lower segment, exclusion and extraperitoneal types of cesarean section are elaborated. The appended bibliography, because of its completeness, is in itself a definite contribution to this subject. In the third chapter, the anatomy and histology of the isthmus and the lower segment, so necessary for a clear understanding of extraperitoneal approach in cesarean section, are lucidly described. The authors contend that the fully developed lower uterine segment originates from both the isthmus and the portio abdominalis of the cervix. The anatomy and histology of the fascia and its relation to the bladder, the lower segment and the peritoneum form the subject matter of the fourth chapter. This is well illustrated by means of line drawings and photomicrographs, and helps to visualize what takes place when these structures are separated from each other during the performance of extraperitoneal cesarean section. Chapter five covers incisions, scars and ruptures of the lower segment. Two types of incisions may be placed in the lower segment, the transverse incision and the longitudinal incision, both of which are discussed, their favorable and unfavorable points being brought out. The authors, who favor the transverse incision state, "In America, despite Phaneuf's contribution, DeLee's persistent advocacy of the longitudinal incision has retarded the adoption of the transverse lower segment incision." They show that Waters and Ricci have adopted the transverse incision in the true extraperitoneal cesarean section. Ruptures of the lower segment in subsequent pregnancies and labors are considered in detail. It is shown that most of the reported ruptures of lower-segment incisions followed longitudinal incisions. The methods of delivery in extraperitoneal cesarean section are treated in the sixth chapter, whereas in the seventh, wound infections and methods of drainage are elaborated. The authors advocate, whenever feasible, draining per vaginam. In the eighth chapter the technics of the extraperitoneal types of cesarean section are explained, and a concise table summarizing the various extraperitoneal technics adds to the value of the presentation. All methods of extra-

peritoneal approach are commented on, and four stand out: those of Latzko and Küstner, both with longitudinal incisions in the lower uterine segment, and those of Waters and Ricci, where the lower segment is incised transversely—the second Latzko operation in America is said to have been performed by James W. Markoe of the New York Lying-In Hospital. Because of the better exposure obtained the operations of Waters and Ricci are consistently gaining in favor in America and are supplanting those of Latzko and Küstner. The procedures of Waters and Ricci are well illustrated; they differ mainly in the method of the separation of the intact peritoneal sac from the bladder in exposing the lower segment. Chapter nine explains the essential factors in the execution of the Physick-Sellheim extraperitoneal cesarean section and is a recapitulation of the technical details elaborated in the previous chapters. The tenth chapter stresses extraperitoneal cesarean in patients previously cesareanized or laparotomized. By means of well-adapted illustrations, the authors show how the difficulty of adhesions may be overcome and how an extraperitoneal cesarean section may be repeated should the occasion arise. Finally, in the eleventh chapter, the operative and postoperative complications, which consist of injuries to the peritoneum and bladder during the dissection, are discussed in detail, and methods for the repair of these injuries are given. Fundal packing and hemorrhage are touched on, as are hematomas and retrovesical phlegmons.

The illustrations throughout this book are carefully chosen and well executed, and one is impressed with the tremendous amount of work required in the extensive compilation of the literature of lower-segment cesarean section. This monograph should prove to be of value to the obstetric specialist and should serve as ready reference for writers on the subject; whereas from a historical standpoint, it should interest all physicians who practice obstetrics.

The Management of Fractures, Dislocations and Sprains. By John A. Key, M.D., and H. Earle Conwell, M.D. Third edition. 4°, cloth, 1303 pp., with 1259 illustrations. St. Louis: The C. V. Mosby Company, 1942. \$12.50.

The appearance of the third edition of Key and Conwell's treatise on fractures and sprains marks an endeavor to produce an up-to-the-minute discussion of subjects than which there are scarcely any of greater importance. New methods are being introduced so rapidly that it is difficult to evaluate their comparative efficiency. Good results are obtained by old and outmoded methods. The important fact to remember is that each case is a law unto itself. There will inevitably be differences of opinion concerning the merits of different technics but, among them all, there will probably be at least one that may be applied to the condition in hand.

The methods set forth in this book are advocated by two authors whose opportunities for studying a large number of fractures and sprains have been extensive, and their opinions cannot be lightly brushed aside. For those who can hospitalize their cases of fracture, where it is possible to take advantage of all the modern facilities for dealing with these conditions, this volume should be of considerable value, since it outlines the authors' experiences in handling a large number of such lesions. One should remember, however, that facility in the employment of modern technics is the key to their satisfactory use. As a reference book for the guidance of such individuals this volume has much to recommend it, although in the management of some types of fracture

there will be divergences of opinion regarding the propriety of certain of the suggestions offered

It is unfortunate that the book is so bulky and heavy which interferes with its convenient use

Administrative Medicine Edited by Haven Emerson MD 4th, cloth, 839 pp., with 39 figures, 82 tables and 16 charts New York Thomas Nelson and Sons, 1941 \$7.50

This book should convince the most skeptical that administrative medicine is worthy of being considered a medical specialty or specialties Dr Emerson's long association with practically all types of medical, medico-social and public health activities has enabled him to develop a comprehensive collection of subjects and to select writers who were not only familiar with their subjects but also forward looking and future minded

The same general plan is followed in presenting each subject First, a short historical sketch of its development, next, a consideration of the present organization and activities, with indications of the trends and then in some cases, definite suggestions concerning future developments

The book is divided into three parts Part I deals with the organized care of the sick, hospitals of all kinds convalescent homes, outpatient service, home care, visiting nurse service and, finally, the latest development, voluntary hospital-care insurance Each author is a master of his subject Part II discusses public-health services International, national, state and local public health organizations are clearly delineated Then follows a series of interesting chapters on what might be termed the public health specialties—vital statistics, communicable disease control, occupational hygiene, milk control and laboratories, to mention only a few Persons who believe themselves well informed will learn much by reading these chapters Part III covers inclusive medical care for prevention and treatment The description of the medical services of the armed forces is particularly complete and clearly set forth, but under the stress of war probably is now undergoing marked changes

The chapters Medical Services under Government Auspices in the United States and Canada and Economic and Social Aspects of Administrative Medicine are complementary, the first setting forth the present stage of development of governmental participation and the latter presenting the arguments for future developments along the line of compulsory health legislation

This book should be most useful as an authoritative, up-to-date encyclopedia on the subjects presented

The Modern Attack on Tuberculosis By Henry D Chadwick, MD, and Alton S Pope, MD 8th, cloth 95 pp., with 5 illustrations and 8 tables New York The Commonwealth Fund, 1942 \$1.00

With the steady decline in the morbidity as well as the mortality from tuberculosis the time has come when the final attack for its complete eradication must be planned with vigor and determination It is with this thought in mind that this book has been written The authors state in their preface that they make no pretense of adding to the sum total of knowledge concerning tuberculosis They believe that sufficient facts are already available to make the eradication of tuberculosis a possibility within a few generations if the established techniques are effectively applied The writers are men of many

years of experience both in the clinical as well as in the public health field and thus can speak with authority and in sure judgment

The worthwhileness of this book is enhanced by its clarity and brevity This small book, divided into six chapters is crammed with information and important facts regarding the final triumph over the age old scourge of tuberculosis The authors' emphasis is centered on the prompt discovery of tuberculous infection and the early segregation and treatment of cases Case finding in the community is the modern watchword of the health worker Although early diagnosis was the goal of the tubercle worker twenty five years ago, his modern counterpart goes out into the field and searches for latent foci of infection in the most susceptible portion of the community Thus the authors urge mass x-ray examinations of tubercles—especially embryo physicians and nurses, patients in prenatal clinics, all contacts and elderly persons They also stress the sanatorium as not only the place for the treatment but also the place for the segregation of infected persons Thus they plead for more sanatorium beds in more attractive surroundings with greater appeal to patients The authors dare to prophesy that the bells that ring in 2000 may sound the death knell of the tubercle bacillus

The scientific and the public health aspects concerning the eradication of tuberculosis are clearly and authoritatively covered in this book It should serve as a useful guide not only to tuberculous workers but also to all interested in community health

Internal Medicine in Old Age By Albert Mueller Deham, MD and S Milton Rabson, MD 8th, cloth, 396 pp., with 10 illustrations Baltimore The Williams and Wilkins Company, 1942 \$5.00

The authors of this book, after a brief discussion of certain general aspects of old age, present internal diseases system by system, as they occur in the aged In consequence of this chosen limitation, two important features of practice among the old—psychologic problems and problems on the border line between medicine and surgery—are omitted In the present state of knowledge of geriatrics, the field should be covered for the practitioner relatively simply Authors of books of this sort however, err in including too many individual diseases concerning certain of which there is nothing of consequence to be said For example, in this book there are discussions of scurvy, agranulocytosis, amebic dysentery and Weil's disease that will not help the physician who deals with the aged as much as those in any standard textbook of medicine Moreover, in this book the authors often recommend treatment that is unacceptable to many physicians in this country transplutinin in pneumonia, creolite, guanacol and tuberculin in tuberculosis, iodides in arteriosclerosis neoraphenamine in coccal or mixed infections of the bladder, interdiction of meat and limitation of other proteins in impending hepatic failure and so forth There is much insistence on the weight of individual experience in rendering judgment on the efficacy of treatment, a form of argument that is least convincing to the critical mind Physiologic mechanisms, such as those of angina pectoris and hypertension, are described but with serious inaccuracy On the other hand, anatomic changes are more richly and more satisfactorily presented than in other available books in this field. It is only for this feature that the book can be recommended

Immunity against Animal Parasites. By James T. Culbertson, B.S., A.M., Ph.D. 8°, cloth, 274 pp. New York: Columbia University Press, 1941. \$3.50.

This monograph by a member of the Department of Bacteriology of Columbia University satisfactorily replaces the second edition of *The Immunology of Parasitic Infections*, published in 1929 by another expert in the field of animal parasitology.

It is divided into three parts. The second part, which deals with immunity in specific diseases, makes up the bulk of this book. With Taliaferro's classic textbook as its point of departure and citing almost all the significant papers issued after 1929, it gives thorough information on natural and acquired immunity against animal parasites.

The third part, consisting of only three of the twenty chapters, will be welcomed by the general practitioner who wants a review of vaccinations and diagnostic tests that are of recognized value.

The first part, although presupposing a knowledge of microbiology, is highly useful for it gives a general introduction to and the fundamental principles of the subject. With a few exceptions, for instance, the form of resistance called "premunition," studies on the mechanisms involved in immunity against animal parasites follow a path that is identical with the one opened up by investigations concerning immunity against pathogenic bacteria. Even ablative antibodies, which have been demonstrated by Taliaferro in immune serums against trypanosomes and by Campbell in immune serums against cestodes, trace their origin to antibodies uncovered in immune serums against anthrax and swine erysipelas. They have also been called "azygots" in order to point out their lack of absorption by homologous antigens. Culbertson, although conceding that ablative antibodies are not absorbable, maintains that their effect is due to their union with the antigens of the parasites. Considering the effort required to gather the heterogeneous literature on this matter, such a logical incompatibility and a few other discrepancies are quite understandable and do not affect the usefulness of this able attempt to give thorough orientation in a specialized branch that had to be worked out in a form accessible to the student, as well as to the practicing physician or veterinarian.

The illustrations, charts and tables have been selected with a didactic flair that will be appreciated particularly by the teachers, who henceforth will have at hand a treatise that they can resort to when lecturing on immunity against animal parasites.

The Principles of Anatomy: As seen in the hand. By Frederic Wood Jones, D.Sc. (Lond., Adelaide and Melbourne), F.R.S., F.R.C.S. Second edition. 8°, cloth, 418 pp., with 144 illustrations. Baltimore: The Williams and Wilkins Company, 1942. \$7.50.

The first edition of this well-known work, published in 1920, was prepared during World War I as part of the course of instruction to officers of the Royal Army Medical Corps to qualify them to care properly for military injuries of the hands. This second edition, similarly a product of war, is brought to date by the addition of six new chapters and twenty new figures in the text.

The author emphasizes topographical and functional anatomy, and uses the hand as an example of an anatomical method that can be applied to other regions. Beginning with phylogenetic and morphologic considerations of pentadactylism and polydactylism, he discusses the comparative digital, phalangeal, metacarpal and carpal formulas of

man and of other animals. Similarly he deals with flexure and cleavage lines, papillary ridges, nails, functions, fascias, bones, joints and sesamoids of the hand. In his study of morphology of the extrinsic and intrinsic musculature, he quotes Dwight's cautioning stricture that "to find in man an occasional form of a muscle that is normal in no matter what animal" does not necessarily explain "how the peculiarity could have been transmitted." Finally he gives in detail not only the vascular and lymphatic channels and arteriovenous anastomoses of the hand but also its somatic and autonomic nerves and the sensory and motor pathways that connect it with the brain. His method is illuminating, his observation accurate, his descriptions detailed, his interpretations conservative. Particularly valuable are his analyses of "trick movements" following nerve injuries.

As a text of applied anatomy, combined with such a clinical work as that of Kanavel, this book is of timely value to military surgeons preparing to treat war injuries of the hands. It is provided with many admirable illustrations and with well-selected references for further reading.

Castor Oil and Quinine: Once a doctor, always a doctor. By George W. Vandegrift, M.D. 8°, cloth, 252 pp. New York: E. P. Dutton and Company, Incorporated, 1942. \$3.00.

This is the biography of a New York physician who practiced from 1879 onward on the lower East Side of the city. The story is written by his son, presumably from authentic evidence received from his father. The elder Vandegrift was a typical "corner doctor." He soon established himself at the junction of two well-known streets, and treated everybody who came to his door for any sort of an illness. It was a rough sort of practice, but the art of medicine has seldom been better exemplified than in the story of this untutored, honest practitioner. The book gives the story of medicine as practiced in a big city and in a ward filled with Irish and German immigrants during the latter quarter of the nineteenth century. Vandegrift's account of his father is interesting and readable, and in many ways may be considered a unique document. The title gives the clue to the type of medicine practiced by this pioneer physician, for he, indeed, was as much of a pioneer as the man who went into the Far West during the early days of the century.

The Care of the Aged: Geriatrics. By Malford W. Thewlis, M.D. Fourth edition, thoroughly revised. 8°, cloth, 589 pp., with 50 illustrations. St. Louis: The C. V. Mosby Company, 1942. \$7.00.

In this edition, as in its predecessors, the author gives some consideration to the practical handling of most of the medical problems of old age. Unfortunately, knowledge of the fundamental characteristics of the aged, which must determine special aspects of their treatment, is fragmentary. As the title indicates, a summary of even this incomplete knowledge is outside the scope of the book. Hence, the uncertainties of geriatrics and the fundamental problems that await clarification and solution receive little emphasis. Furthermore, the book seems to slight the psychologic aspects of disease and treatment in old age. Since the author undertakes to deal with a wide range of diseases, it is to be expected that specialists will disagree with his advice in not a few instances. Nevertheless, the practitioner will find this the most helpful book in the field.

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VASCULAR AND NEUROLOGIC LESIONS IN SURVIVORS OF SHIPWRECK*

I. Immersion-Foot Syndrome Following Exposure to Cold

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BOSTON

As a result of enemy submarine activity, many survivors of torpedoed vessels have been exposed to unusual physiologic conditions. These include cold air and water and, when rescue is long deferred, prolonged dependency of the legs, malnutrition and vitamin deficiency. Many of these men have required hospitalization in naval and marine hospitals. One of the commonest in incapacitating lesions is painful swelling of the feet and lower legs. This condition has been called "immersion foot." It has been my privilege to study it in Scotland and along the western Atlantic seaboard from Nova Scotia to Virginia. A surprising feature is that painful swelling of the lower extremities may take place both after exposure to the cold of the North Atlantic winter and the warmth of the Gulf Stream in southern latitudes in April and May.

The purpose of this paper is to point out that in the true immersion foot syndrome, which occurs after relatively brief exposure of the lower extremities to cold water, there is actual thermal injury to the skin and subcutaneous tissue, whereas in the survivors of prolonged exposure in southern waters this feature is not present, but the painful swelling of the dependent parts is caused by a systemic disturbance.

CLINICAL OBSERVATIONS

Immersion foot, caused by prolonged chilling just short of actual freezing, has not heretofore received adequate recognition, although it must have occurred after torpedoings in the last war and after shipwreck in northern waters since time immemorial. An excellent clinical picture has recently been given by Webster, Woolhouse and Johnston,¹ the Canadian naval medical officers who have treated by far the largest number of cases. According to them:

At the time of removal of the patients from the open boats or rafts, the feet were cold, swollen and waxy

white in color, with scattered cyanotic areas. The patients complained at that time that their feet felt heavy, 'woody' and numb, and the feet were anesthetic to pain, touch and temperature.

Shortly after removal of the feet from this traumatic environment, the swelling increased rapidly as the feet became red, hyperaemic and hot without sweating, and the pulse in the vessels of the feet was full and bounding. In those more severely damaged areas—usually the toes, the distal part of the dorsum of the foot and the ball of the foot—the parts remained oedematous and hot, and assumed a livid, cadaveric appearance. A number of these latter areas later produced blebs, some of which were filled with straw-colored fluid and others with extravasated blood, and areas of ecchymosis commonly appeared over the medial aspect of the first metatarsophalangeal joint and on the medial aspect of the longitudinal tarsal arch. Many of these feet presented the appearance of incipient massive gangrene. The rapid swelling and increasing redness, accompanied by the extreme rise in temperature of the part, presented the picture of an intense vasodilatation, accompanied by definite damage to the vascular wall with transudation, as manifested by bleb formation and extravasation of blood.

The anaesthesia followed a variety of patterns. In the mildest cases these areas extended around the margins of the foot and over its plantar aspect, being of greater extent along the lateral border, where the mass-to-surface ratio is smallest. In the more severe cases these areas extended over the entire dorsum of the foot, and in some cases over the lower two thirds of the leg. Patches of anaesthesia over the knees in the prepatellar and infrapatellar regions were observed in two cases where there had been prolonged kneeling in the lifeboats.

Attention was first focused on this syndrome by the Medical Corps of the Royal Navy after the loss of a ship off the northern Norwegian coast in the late spring of 1941. The ocean temperature was around 40°F. A number of the crew were adrift on Carley rafts for several days. These rafts are large, doughnut-shaped floats with an open lattice in the center. The occupants are therefore forced to sit on the floating outer hull and keep their feet immersed in the cold water that washes in

*Released for publication by the Division of Publications, Bureau of Medicine and Surgery, United States Navy.

and out of the bottom. After these survivors were rescued by trawlers (which carry no medical officers), the mistake was made of rapidly warming their numb and swollen feet before the galley stove. Three months later, when I visited the naval hospital at which they had been treated, the last of these patients was being discharged. From the description given me by Surgeon Rear Admiral Sir William Wheeler and from the recently published account by Ungley,² the vascular and neurologic changes in the immersed extremities were identical with those of the Halifax survivors that are described below, except for their greater severity. Owing to the unfortunate rapid warming before the galley stove, a number of these men developed gangrene, which necessitated amputation. The others suffered from trophic disturbances of the skin and neuritic pain, which prevented their return to active duty for a very protracted period. The severity of the process and the prolonged period of convalescence illustrate the need of efficient first-aid and subsequent hospital treatment.

During the past winter over 100 similar cases have been treated in Halifax. Through the kindness of Surgeon Commander D. W. Johnstone, the senior medical officer of the Canadian Navy there, I was given every facility to examine 32 survivors of three vessels torpedoed in the North Atlantic early in March, 1942. These patients were under the charge of Surgeon Lieutenant Commander D. R. Webster, Surgeon Lieutenant F. M. Woolhouse and Surgeon Lieutenant J. L. Johnston, who were extremely co-operative and helpful. A description of their cases has just been published by them.¹ The reason for presenting this brief résumé of their work is twofold: first, to add observations on 15 other cases seen at the Halifax Infirmary, with the senior surgeon, Dr. Alan Currie, at the Columbia Medical Center, with Dr. David Bull, and at the United States Naval Hospital in Chelsea; secondly, to contrast these cases of immersion in cold water with a series of superficially similar, but fundamentally quite different, results of more prolonged immersion in warm water seen at the United States Marine Hospital in Norfolk during May, 1942. The latter group will be taken up in the second part of this paper.

The 32 patients seen in Halifax were exposed to air and water close to freezing temperature in three lifeboats for periods ranging from twenty-seven hours to four days. In all cases it had been impossible to keep the boats bailed dry, so that water was sloshing about over the floor boards from a depth of a few inches up to the height of the thwarts. The men's legs were therefore con-

stantly wet below the knees and actually immersed most of the time from the ankles down in cold water. The reaction of the lower extremities to cold and wet was greatly aggravated by the fact that they were continually dependent and that, on account of crowding, there was no opportunity to exercise or elevate the legs (see below, section on "General Responses of Tissues to Cold"). Whether the survivors wore shoes or not made little difference, as the wet feet became so swollen that any boot soon became tight and constricting. The feet under these conditions rapidly became numb, painless and cadaveric in color. A few of the men tried at first to keep out of the water, but soon gave up. Only in the rare cases where men had on loosely fitting rubber hip boots and managed to keep their feet relatively dry, or where they were able to wrap them in a blanket and keep them clear of the water for the better part of the time, were they able entirely to avoid this condition.*

On being picked up by rescuing vessels, those who suffered from immersion foot observed that it felt as though they were "walking on air" or "on blocks of wood." The more severely afflicted men could not maintain their balance or walk, and had to be supported or carried. On arriving in warm quarters below decks, their feet were so swollen that if boots had been kept on they usually had to be cut off. The extreme swelling and gray, cyanotic hue of the severe cases made it look as though many might develop gangrene of the feet. Fortunately, the mistake made in the first-aid treatment of the British survivors reported above was not repeated here. None of these men had their numb feet soaked in hot water or warmed before a galley stove. Some had them immersed in cold water for a brief period, others rubbed with alcohol (even this was a mistake; see below, section on "Treatment"). They were then put in bunks and given hot drinks. In the milder cases the feet began to tingle and burn as soon as they warmed up, but those more severely chilled remained numb for much longer periods.

On reaching Halifax it was observed that the feet, which at the time of rescue had been cadaveric in color, cold and numb, were pink, hot and painful, as in erythromelalgia. The edematous skin was dotted with petechial hemorrhages and, in the severer cases, with large blisters that resembled those of a superficial burn. Sensation,

*Since this article was written I have had the opportunity of examining 8 members of the crew on a torpedoed merchantman after three days adrift in cold water. Three of these men had been protected by a new type of rubber lifesuit and suffered no thermal injuries, whereas the remainder who wore ordinary clothes, all developed immersion foot of moderate severity.

which at first was absent above the ankle, usually descended to the midfoot within a period of twenty-four hours, although the toes often remained anesthetic for a period of several weeks (Fig. 1). With the partial return of sensation,

tion secondary to epidermophytosis eventually necessitated their amputation. Eight patients showed edema, blebs, petechiae and superficial patches of gangrene from their severe chilling (Cases 2, 3, 4, 6, 7, 8, 18 and 19). Thirteen men (including all

Moderate hyperemia and anesthesia, without much cutaneous injury, 2 weeks after rescue.
 Appearance of feet: Redness of skin and petechial hemorrhages
 Redness most striking in dependency Very slight residual swelling. Superficial loss of epithelium on soles
 Arteries: All pulsations strong
 Veins: Very prominent
 Sweating: Began slightly over skin of proximal feet at 13 days
 Neuritis: +++, beginning to subside

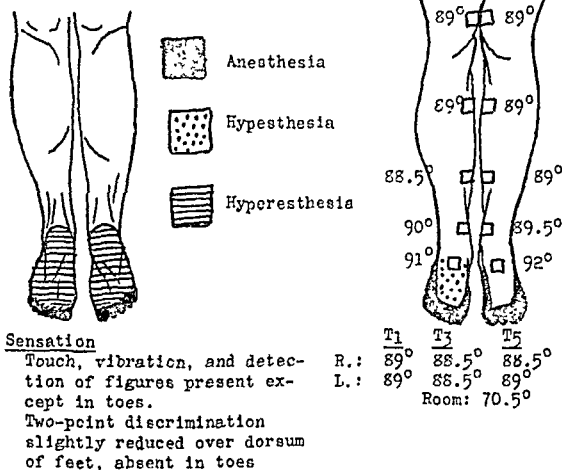


FIGURE 1 Case 10

burning, tingling pain became intense and, together with the risk of the blebs' rupturing and becoming infected, presented the major therapeutic problem. These clinical findings seen in the Halifax cases are summarized in Table 1 and illustrated in Figures 2 and 3.

Examination of Table 1 shows that of the 19 acute cases of true immersion foot examined in detail, only 2 developed areas of gangrene of sufficient depth to require surgery. In Case 19 bilateral major amputations were necessary, owing to the cellulitis that followed the prolonged severe exposure and was already present when the patient reached the hospital. The infection entered through the blisters that always develop after long immersion in cold water. In Case 1 the loss of tissue involved several of the small toes, and late infec-

tion secondary to epidermophytosis eventually necessitated their amputation. Eight patients showed edema, blebs, petechiae and superficial patches of gangrene from their severe chilling (Cases 2, 3, 4, 6, 7, 9, 10, 11, 12, 13 and 18), particularly in the first two weeks. At the

end of this period the active inflammatory process was usually subsiding, and the skin of the sole and toes desquamating in large sheets. In cases with inadequate early treatment, both swelling and

surgeon-general of Napoleon's army in the winter retreat from Moscow. In the Crimean War⁴ it was observed that the soldiers suffered most in temperatures just above freezing in the wet mud and



FIGURE 2 Case 1

The photographs were taken on the twelfth day after rescue. The man had been in a lifeboat without shoes for four days in the North Atlantic in March. The temperature of the sea water was recorded at 34° F., and his feet had been wet most of the time. On arrival in Halifax the hyperemia and vascular engorgement of the lower legs were intense; his feet were greatly swollen, blistered and anesthetic; his toes were blue-black and gangrenous looking. After treatment by cooling for twelve days in ice-packs, the swelling was greatly reduced, the blebs had nearly absorbed, and the condition of the toes was distinctly improved. Nerve recovery had not progressed far enough to cause pain.

pain tended to persist and become a cause of prolonged disability (up to six months).

A number of late complications have been observed in consultation with Drs. A. W. Stearns and R. S. Schwab at the United States Naval Hospital in Chelsea, and with Dr. D. C. Bull at the Columbia-Presbyterian Medical Center in New York City. These include atrophy of the intrinsic muscles in the feet (2 cases), a chronic sense of bursting fullness in the lower legs in patients who had varicose veins (3 cases) and various stations of psychoneurosis (8 cases). These are outside the scope of this paper.

GENERAL RESPONSES OF TISSUES TO

Before discussing the important subject, it will serve to orient one's concept, regard to review what is already known of the fundamental responses of the tissues to the pathologic changes that take place after severe chilling and immersion. On the literature, it is by the fact that there is no fundamental pathologic difference in the various responses to cold. There is a commonality to injuries due to both immersion and with Baron Larrey's⁵

snow of the trenches, particularly when unable to move about. Even then it was recognized that fatigue, stagnation of circulation, constriction of the legs and scurvy were important accessory factors. Greene,⁷ who as medical officer of two Himalayan expeditions had an unusually wide experience, has written a most timely account of the injuries that follow various forms of exposure to cold. He describes the trench-foot syndrome of the last war, which is essentially identical with that of immersion foot. Numbness gradually develops in cold, wet, dehydrated extremities, and is followed by swelling and blisters. When the blisters rupture, streptococci may bring about widespread gangrene, as well as in the prolonged exposure. It also is a descriptive term for the condition in lifeboats as the exposure is to break and pain in trench foot, which is in period of said shelters. The condition when the the bar of shiny and dry from vitamin

deficiency) are important accessory factors. Greene makes a brief reference to immersion foot, but states that he has never seen a case of it. The first comprehensive reports on this syndrome have been

is -1.9°C , it is obvious that, in immersion foot, actual freezing does not take place.

In investigating trench foot in the last war, Smith, Ritchie and Dawson¹⁰ carried out an ad



FIGURE 3 (1 of 2)

This seaman was in the same lifeboat as the man whose feet are shown in Figure 2. He also had no shoes, but his local injury from cold was much less pronounced. He was able to walk, and on admission to the hospital his feet were only slightly swollen, with hypesthesia of toes and intense hyperemia. Pain was severe, but after ten days' treatment in ice packs, circulation had returned to normal and the pain was no longer present so long as his feet were exposed to the cool air of the ward. The patches of gangrene shown in the photographs, taken on the twelfth day, were only skin deep.

published recently.^{1, 2} In addition, previous clinical and laboratory investigations are of value in understanding the underlying features of the condition.

The effects of cold with special reference to frostbite were studied by Rischpler⁷ in 1900. He froze animal tissues by the application of ice and salt, and investigated the results microscopically at various intervals. Under these circumstances actual degeneration was found in the cells of the blood vessel walls, with swelling of the connective tissue and vacuolation of the smooth muscle fibers, but there was no sign of thrombosis. During the last war, Luke⁸ found that the critical temperature where all metabolic processes are inhibited is -6°C (21°F). He claims that at this temperature blood freezes with destruction of cells liberating thrombokinase, and that on thawing thrombosis occurs. More recent studies by Lewis⁹ show that this is not necessarily true. Although the freezing point of blood is -0.53°C , and that of the tissues close to this level, Lewis found that skin when cold rarely freezes at its true freezing point. It exhibits the property of supercooling and may not freeze until the temperature falls to much lower levels, -20°C (-4°F). As the freezing point of sea water itself

is a mirable set of animal experiments under conditions that closely resemble those resulting in immersion foot. They subjected rabbits in a cold chamber to standing on wet mud. When this was continued for three days, especially after removing the fur from the paws, marked swelling of the feet resulted. Histologic examination showed changes in the blood vessel walls, with an outpouring of fluid containing both cells and fibrin. Occasionally the nerve trunks showed diffuse swelling of the axis cylinders, but without evidence of degenerating fibers in preparations stained by the Marchi method. The investigations thus proved that simple prolonged exposure to cold can produce subacute inflammation of the skin and subcutaneous tissues of the feet. These changes could be exaggerated by moisture, by applying constricting bands to the upper legs and by rapidly warming the chilled extremities before the animals were sacrificed.

The most illuminating discussion of the pathologic physiology of tissues exposed to cold is contained in a series of three lectures delivered by Sir Thomas Lewis¹¹ in 1941. On exposure to cold the blood vessels are constricted both by vasoconstrictor impulses from the hypothalamus and by direct contraction of the smooth muscle

TABLE 1. *Summary of Findings in Cases of Immersion-Foot Syndrome (Northern Survivors).*

CASE No.	TISSUE DAMAGE ON ARRIVAL AT HALIAX	FIRST SENSATION	PAIN		SENSORY LOSS	SWEATING	HYPEREMIA	TREATMENT	
			SEVERITY	DURATION				TYPE	DURATION
1	Swelling and blebs ++; gangrene of several toes.	Still absent	?	?	Distal half of feet	Absent below ankles	+++	Continuous ice packs Later, amputation of several toes	12 days
2	Swelling and blebs +; patches of cutaneous gangrene.	4 days	++	Subsiding	Toes	Normal	+++ (10 days)	Continuous ice packs Exposure to air	10 days 2 days
3	Swelling and blebs ++; small petechiae.	5 days	+++	Beginning to subside	Distal third of feet	Absent below ankles	+++	Intermittent ice, air and electric fan	12 days
4	Swelling and blebs +; petechiae.	—	++	Beginning to subside	Toes	Absent lower feet and toes	+++	Intermittent ice, air and electric fan	12 days
5	Slight	—	+	Beginning to subside	Toes	Absent lower feet and toes	+++	Exposure to air	12 days
6	Swelling and blebs +	2 days	++	Still present	Toes (hypesthesia)	Absent lower feet and toes	+++ → +	Continuous ice packs	12 days
7	Swelling and blebs +	1 day	++	Still present	Toes (hypesthesia)	Normal	0	Exposure to air	12 days
8	Swelling and blebs +	1 day	++ → +	Subsiding	Almost gone	Normal	+	Exposure to air	12 days
9	Swelling +	3 days	++	Still present	Almost gone	Absent lower feet and toes	+++ → +	Continuous ice packs Exposure to air	13 days 1 day
10	Swelling +	10 days	+++	Increasing	Distal third of feet	Normal	+++	Exposure to air Intermittent ice packs	12 days 2 days
11	Slight	1 day	++	Subsiding	Toes (hypesthesia)	Normal	0	Exposure to air	12 days
12	Slight	12 hours	+ → ++	Still present	Toes (hypesthesia)	Increased	0	Exposure to air	12 days
13	Slight	1 day	+ → ++	Increasing	Toes (hypesthesia)	Normal	+	Continuous ice packs Exposure and elevation	3 days 10 days
14	Slight	3 days	?	?	Distal third of feet	Normal	+++	Continuous ice packs (right), exposure to air (left)	1 day
15	Slight	6 hours	+	?	Feet (patchy areas of hypesthesia)	Normal	0	Exposure to air	1 day
16	Slight	Never lost	Slight	?	0	Normal	0	Exposure to air	1 day
17	Slight	Never lost	Slight	?	0	Normal	0	Exposure to air	1 day
18	Swelling and blebs +; petechiae.	12 hours	+++	Still present	Distal half of feet	Absent below ankles	+++	Intermittent ice packs Exposure to air	14 days 1 day
19*	Cellulitis and septic gangrene of feet	—	—	—	—	—	—	Early amputations	

*Patient seen four months after rescue; reaction to immersion altered by infectious gangrene, which came on during thirteen days' exposure.

cells in their walls. But when the temperature of the skin drops near to freezing, there is an intermittent increase in blood flow, which serves to maintain the viability of the skin. This phenomenon is carried out by a special mechanism of arteriovenous anastomoses (Grant and Bland¹²) and is mediated by local axone reflexes. How long this mechanism can maintain its efficiency in the cold is not known, and it seems probable that the circulation must be reduced to a low point. Lewis observed that immersion of the normal hand or foot in water at 5°C. (41°F.) for as short a period as two hours resulted in definite swelling. This swelling, which may amount to as much as a 15 per cent increase in volume, is not the simple result of imbibition of water by the skin, since it happens in a hand protected by grease or covered by a rubber glove. If swelling of this degree can occur after a few hours, it is obvious that large amounts of fluid must be lost from the circulation on prolonged general exposure. The reduction in the circulating blood volume is the cause of the somnolence and death that overtake so many seamen in lifeboats during severe winter weather. Lewis considers this response to cold to be caused by an "H," histamine-like substance released from the injured cells and acting on the blood vessels.

When the chilled extremity is removed from ice water, the invariable response is a state of hyperemia. The local reddening, vasodilatation and extravasation of fluid from the injured vascular bed are all part of Lewis's classic "triple response." The wheal which first forms may be replaced by a blister. These changes together constitute a simple acute inflammation. Sections of human skin examined by Lewis twenty-four hours after chilling displayed edema of both epidermis and dermis, and a perivascular infiltration of the superficial layers of the dermis with lymphocytes, extravasated red blood cells and some polymorphonuclear leukocytes. Observations now completed in Halifax on many cases of immersion foot show that this inflammatory hyperemia reaches its height on about the third day after the period of exposure is ended and gradually disappears in the course of a fortnight, much as occurs in any other sterile inflammatory reaction.

The changes that occur in the nerve trunks and the terminal superficial axones to the skin are a second point of particular interest. These patients at first have complete cutaneous anesthesia below the ankles. In the mild cases this clears rapidly on warming, but in the severe ones there is still anesthesia of the toes at the end of a fortnight and reduced sensation over the remainder

of the foot. The speed at which sensory recovery may take place over the dorsum of the foot is too great for nerve regeneration and is evidence that the majority of nerve fibers never actually degenerate. This fits in with Smith, Ritchie and Dawson's¹⁰ observations in rabbits' feet after seventy-two hours' exposure to cold. They found definite swelling of the axones, but no evidence of their degeneration. However, in some of the patients of this series (Cases 1, 3 and 10) the toes were still anesthetic at the end of a fortnight and there was little sweating below the ankle. This suggests actual degeneration of the sensory and sympathetic axones to the more exposed distal portions of the feet, which may require a period of several months for complete regeneration and restoration of normal function. In Ungley's² recent report on the Scottish cases, Wallerian degeneration of some of the cutaneous nerves was observed by Blackwood, who examined the biopsies. It is a well-known fact that a partially injured nerve is likely to produce a painful neuritis, and this has been the universal experience in the severe cases of immersion foot. Accurate objective determinations of the recovery of nerves can be made by testing the return of sweating by the method recently described by Minor¹³ and by Guttman¹⁴ at Oxford, and the changes in electrical skin resistance (Richter and Woodruff¹⁵). These methods will be utilized when suitable patients are available in Boston.

The fact that patients continue to suffer after their circulation has returned to normal suggests that the pain is neuritic in origin. This is the most logical explanation in the late stages, but during the acute phase of the reaction this may not be the entire reason. In this connection it is of interest to quote the impression of Webster and his colleagues¹ that these men are comfortable when their foot temperature is kept below 80°F., but that as soon as the ice packs are left off and the cutaneous temperature of the toes is allowed to exceed 90°F. they again experience pain. This fits in with the observations made by Freeman¹⁶ on legs with threatened gangrene. By plethysmographic studies of blood flow in sympathetomized extremities, he has demonstrated that a rise with local heating is caused solely by the increased metabolism of the tissue cells and their need for more blood and oxygen. Local cellular metabolism, like other chemical reactions, should double or treble the consumption of oxygen for each 20°F. rise in tissue temperature. This chemical vasodilatation is not active at temperatures below 85°F., but increases rapidly at higher levels. As a result, if the supply of blood to the tissues is not correspondingly increased, the cells must suffer

oxygen want and this is invariably a cause of pain. Whereas the blood flow through the main pedal vessels is increased tremendously during the phase of acute hyperemia, there is good evidence that the cutaneous arterioles and capillaries have been injured and that therefore there may be a disparity between the supply and the demand for oxygen on the part of the tissue cells surrounding the cutaneous network of sensory nerve endings. On these physiologic grounds moderate cooling of the skin that is involved in a sterile inflammatory process will reduce the metabolic demand for oxygen. If demand can be made commensurate with supply, pain will be alleviated. Lewis¹⁷ stated that spontaneous pain occurs in skin rendered hyperalgesic by heat and other types of injury, and that it is enhanced by warming and relieved or abolished by cooling. Both these factors constitute strong arguments for therapeutic cooling of hyperemic painful feet during the early stage of the post-immersion reaction. Actual experience has borne this out, as it has been found that reducing the cutaneous temperature to 80°F. gives consistent relief in the acute stage.

From a consideration of the above facts concerning the reaction of the tissues to cold, it becomes evident that the common denominator in all conditions that follow thermal insults is injury to the blood vessels and nerves. As Lake⁸ pointed out, "a vicious circle is set up, for the greater the exudation the greater the venous obstruction, and the greater the venous obstruction the greater the rise in capillary pressure, and hence the greater the exudation."

TREATMENT

Prophylaxis

All ship's officers and seamen should be acquainted with the dangers of exposure to cold air and water. When there is sufficient time before abandoning ship, all hands should get into the most waterproof and loosely fitting boots they can obtain and take along extra pairs of heavy socks. If waterproof boots ship water and are wet inside, much can be accomplished by emptying them out periodically and putting on another pair of socks. This is the case even when the socks have been previously wet, provided they are wrung out and partially dried. Much can be done to prevent frostbite of the hands and feet by greasing the skin. Lewis⁹ pointed out that the property of "supercooling" is abolished by wetting and washing the skin, but is greatly enhanced by greasing. A further point to remember is that men in crowded lifeboats must remain fairly immobile, with their legs dependent. Movement of

the cold, benumbed extremities, even temporary elevation, and avoidance of constricting pressure on the legs from clothing or boat gear are helpful factors in preventing severe injury.

First-Aid

When shipwrecked survivors are picked up after prolonged exposure to wet and cold, they should be lifted aboard the rescuing vessel and carried below if their feet are numb, in order to prevent further injury to the anesthetic skin. The possibility of a severe reactive hyperemia and subsequent neuritic pain in the feet must be anticipated, even if actual gangrene from freezing has been avoided. These men require treatment for general as well as local chilling. Methods for dealing with the former are simple and well established, but while external and internal heat is being applied as a first-aid measure to the body as a whole, it should be borne in mind that the chilled extremities will suffer if they are warmed with equal rapidity. It is vitally important, therefore, to warm the patient as a whole first and prevent the chilled, bloodless extremity from increasing its metabolic demand for oxygen more rapidly than it can be supplied by a tardy restoration of the peripheral circulation. Although an appreciation of the risks of warming chilled extremities has been handed down as part of the folklore of the Eskimo, and the danger of this procedure was clearly understood by Larrey³ over a century ago, it is not generally recognized by seamen today.

Whether a person has suffered actual freezing or the less severe chilling seen in immersion foot may not be at first apparent, but in either case the immediate local treatment is the same. It should consist in keeping the exposed extremity cool, elevated slightly above the level of the heart and surgically clean. There is no previous medical experience to point out the most effective methods of attaining these ends, and whatever methods are proposed here will undoubtedly be modified and improved. As local first-aid treatment on shipboard I suggest the following:

1. Give the skin of the feet a preliminary cleansing with soap and cool water. This is to remove superficial dirt and bacteria, which may cause infection of the blisters and thus open the way to cellulitis and moist gangrene. Surgical cleanliness should be scrupulously maintained until the blebs are resorbed and the danger of infection is past. If the blisters have ruptured, do not apply any antiseptics. Dust these raw areas with sulfanilamide powder or cover with sulfathiazole ointment, but if neither is available leave

them alone. On transferring these patients to a hospital ashore, the feet can best be protected against bacterial contamination from blankets and handling by covering them with a sterile towel or bandage (if available), or clean cotton socks.

2. Keep the feet cool by exposure to the room air. Have no bedclothes below the knees, the room cooled below 70°F., and, if possible, direct cool air from a blower or electric fan over the exposed feet and legs.

3. Avoid pressure points on the feet, especially the heels, and elevate the feet on a pillow. Under no circumstances permit these patients to sit up with their legs dependent, as this increases swelling. Elevate the legs so that the feet will be above the level of the heart and thereby promote drainage of edema fluid. Remember that anesthetic, swollen feet are vulnerable to trauma and infection. For this reason even gentle rubbing or massage is dangerous.

4. Use codeine or morphine as necessary to control pain.

Hospital

On arrival in the hospital, the severe cases have pronounced swelling, blebs and discoloration. They have the greatest amount of anesthesia and, for the first few days, the least pain. Hyperemia is striking, with dilatation of the main arteries and prominent veins, but circulation through the cutaneous arterioles and capillaries is nevertheless inadequate, as shown by a dusky cyanotic color and minute hemorrhages in the skin. As explained above, the rationale of treatment at this stage is to reduce tissue metabolism to a point where there is an adequate supply of oxygen to all the cells. This can be accomplished by cooling the skin 5 to 10°F. — to a point below 85°*. Experience has already shown that, under these conditions, color improves, blebs tend to resorb, and edema is reduced.[†] In the mild cases this degree of cooling can be brought about by simple exposure to room air, provided the ward temperature is kept below 70°F. Slightly greater chilling can be obtained by having an electric fan on a bedtable blow air over the feet (Fig. 4), and this can be rendered more effective still if the patient occasionally sprays water from an atomizer into the stream of air from the fan.

Lake deserves the credit for being the first to suggest treatment by controlled cooling. In 1917 he wrote, "It would appear better to keep the limb cool by the application of wet cloths, until efficient treatment can be given, than to allow partial warming to occur." The Halifax experience has, however, demonstrated that wetting the skin is deleterious because it causes maceration.

†This is also true in an experimental burn. Drs. Oliver Cope and George Meier, Jr.,¹² have shown that cooling the burned leg of a dog to 50°F. reduces edema formation to a striking degree, with a corresponding reduction in vascular extravasation and lymph production.

During the most intense stage of hot, congested feet, and also when the neuritic pains are severest, neither of the above measures is effective. The naval medical officers in Halifax have worked out a very satisfactory type of ice pack for use under these circumstances. This consists of a cotton hand

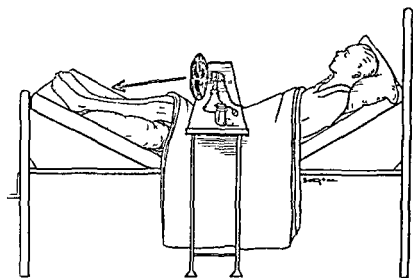


FIGURE 4 Method of Cooling Feet by Exposure to Room Air Supplemented by Electric Fan.

Note that the legs are elevated and that the heels are protected from pressure by a pillow under the calves. The injection of a fine spray of water into the revolving fan blades with an atomizer further increases the cooling.

towel to cover the foot; four ice bags applied over the dorsum, soles and sides of the foot; oil-silk wrappings to 12 cm. above the malleoli; a thick insulating pad of fluffed cotton or cellulose; and a rubber pillowcase tied loosely about the calf of the leg. The purpose of this pack is not to induce severe chilling, which might lead to further trophic disturbances, but to cool the skin of the foot and toes to a level between 80 and 85°F. During the early, intensely hyperemic stage a thermocouple inserted next to the skin shows that the temperature of the foot does not fall below 90°F., although the toe temperatures may drop 5 to 10° farther. At this period the active circulation causes rapid melting of the ice. The packs should be changed at four-hour intervals and observations of skin temperature made at these times to control their application. In Case 2 the feet maintained this intense hyperemia in continuous ice packs for the first eleven days, but on the twelfth day of treatment they became distinctly cool. The ice packs were then discontinued and treatment by exposure to cool air begun.

From this point on the patient can usually be made comfortable by simple exposure of his legs from the knees down, supplemented if necessary by a breeze from an electric fan as mentioned above. At night, however, the neuritic pains may increase in intensity. The patients appreciate the

value of the ice packs for relieving pain and often request their reapplication. Under these circumstances a less elaborate pack is usually sufficient, consisting of a cotton towel to cover the foot, two ice bags on the dorsal and plantar surfaces and a large bath-towel wrapping.

In carrying out treatment with ice packs it is important to make sure that they do not leak and wet the skin. Each time this has occurred it has caused soggy and maceration.

In all the patients tested during the hyperemic stage, and even when it was subsiding, hanging the feet over the side of the bed caused striking congestion and pain. Conversely, elevation made the feet more comfortable. Many of the men discovered this for themselves and elevated their legs at the time of painful crises. The elevation need not exceed 20°. This is the best position for patients who are being treated by simple exposure of the legs to cool air, with or without an electric fan (Fig. 4).

On a theoretical basis, I advocate a period of Buerger's exercises prior to getting the patients out of bed. In these exercises, which are so useful in cases of threatened gangrene from arteriosclerosis or thromboangiitis obliterans, the feet are first hung over the side of the bed for four minutes, while the patient exercises the foot muscles by dorsiflexion and plantar flexion, inversion and eversion at the ankle and then flexion and extension of the toes. The feet are next elevated 45° for one minute, and then rested flat on the bed for five minutes. Cycles of these exercises carried out for half-hour periods three to four times a day should be tried as soon as the patient can tolerate the dependent position, and continued conscientiously for a week before permitting him to get out of bed.

Another measure often helpful in the early stage of edema and neuritic pain, particularly after prolonged exposure with starvation, is a diet high in protein and vitamin B. This is of specific value in survivors who have been adrift for long periods on a deficient diet, as will be shown in the second part of this paper.

On the basis of the similarity between the swelling due to immersion in cold water and that secondary to a burn, Koch's¹⁹ method of compression dressings might be a valuable adjunct in treating patients with particularly severe edema and bleb formation, provided hyperesthesia of the skin is not a major complication. I hope to have the opportunity to give it a trial this coming winter. However, in view of the fact that thermal injuries from cold often have associated cutaneous anesthesia, care will have to be used in applying a tight dressing, in order to avoid trophic ulceration.

Operations for Relief of Pain and Vasospasm

Smithwick and White²⁰ have advocated crushing the peripheral nerves through small incisions above the ankle for the relief of intractable pain in cases of peripheral vascular disease. This operation has been extensively employed during the past twelve years and has proved valuable. When the nerves regenerate, as they do regularly in three months, they do so without pain. Such a procedure should also be of value in the control of the neuritic pain of immersion foot, provided cases occur with such severity that the methods given above prove inadequate. To test this out I injected the posterior tibial and the superficial and deep peroneal nerves in Case 10 with a 2 per cent solution of procaine and found that the patient obtained complete relief for a period of two hours. Nerve crushing should be reserved for the severe cases, as it will incapacitate the subject for duty for three months, the period required for full regeneration of the nerves.

Blocking the sympathetic outflow to the lower extremities by therapeutic paravertebral injections of procaine hydrochloride and by lumbar sympathectomy has been suggested by a number of French and American surgeons, notably Leriche,²¹ Simon and Filhoulaud,²² Soupault and Orsini,²³ Forster and Wiederkehr²⁴ and Veal and Klepser.²⁵ I am unable to see how any possible improvement can result from such procedures during the acute stage. Absence of sweating proves that the terminal vasoconstrictor fibers are already interrupted, and the local hyperemia is more intense than that produced by sympathectomy. Indeed, the suggestions of Lewis and Love²⁶, and of Lake⁸ that steps should be taken to constrict the main arteries seem more rational. As Greene⁵ has stated, "it is to be hoped that without careful previous animal experiments no surgeons will be tempted to follow in the footsteps of these French colleagues." To see if the pain of immersion foot could be relieved by interruption of the sympathetic vasoconstrictors, I blocked the lumbar ganglia with procaine in Case 10. The patient's pain was not influenced in any way, but as I am not convinced that the sympathetic pathways were entirely interrupted, the test should be repeated. On the other hand, procaine injection of the posterior tibial and the superficial and deep peroneal nerves above the angle in the same patient abolished the pain completely.

The only case where lumbar sympathectomy is likely to be of value is in the late stages when the circulation of the foot remains insufficient. Four of the Halifax patients after recovery had unusual

ly cold and sweaty hands as well as feet—a mild variety of Raynaud's disease. One of these (Case 19) who had had a Syme's amputation, continued to be incapacitated by ulceration at the end of the stump. He was tested by procaine block of the vasoconstrictor fibers (both by lumbar paravertebral and by subarachnoid spinal block), but showed no appreciable rise in cutaneous temperature in the ulcerated area. This was evidently due to organic narrowing of the peripheral vessels, secondary to his unusually prolonged chilling and septic gangrene. Nevertheless, cases will undoubtedly occur, as has already been observed in frostbite, where an inadequate circulation in the late stages of severe immersion foot (with secondary arterial occlusion) can be benefited by lumbar sympathetic ganglionectomy. A number of such patients, who six months after their initial exposure are still suffering from cold and pain in their feet, are under investigation at the United States Naval Hospital in Chelsea at the present moment. In addition to the inadequate circulation of their feet, the presence of increased sweating and of vasomotor changes in their hands indicates that they have an underlying vasomotor syndrome. Although it is unlikely that this condition originated with the exposure, it was probably increased by the psychic trauma.²⁷ Permanent vasodilatation may well result in secondary relief of the deep plantar pain.

PROGNOSIS

Although it is too early to give accurate statistics of the end-results in immersion foot, it appears that the majority of patients respond favorably to the methods of treatment described above and should be able to return to duty within a month or six weeks. In the rare cases where gangrene develops or there is pre-existent peripheral vascular disease, and particularly when the sufferer has the misfortune to develop a psychoneurosis, convalescence may be very protracted.

SUMMARY AND CONCLUSIONS

Immersion foot, secondary to exposure to cold, appears to be caused by sublethal injury to the chilled tissue cells, the cutaneous arteriolar and capillary bed and the nerve fibers. The process differs only in the degree of chilling and wetting from frostbite, trench foot and shelter foot.

The ischemia during prolonged exposure to intense cold is followed by a period of acute inflammation. The hyperemic reaction of the feet is due mainly to the chemical effects of the products of tissue injury. Paralysis of the vasoconstrictor fibers is an added factor, but is of secondary importance.

In spite of the increased flow of blood in the main vessels, there is a disparity between the blood-oxygen supply and demand in the cutaneous capillary bed. Capillary permeability is thereby increased. Edema, pain and petechial hemorrhages, as well as the congestion seen when the feet are in the dependent position, are evidence of injury to the blood vessels. By cooling and reducing the local metabolism and need for oxygen, both edema and pain are diminished.

The inflammatory reaction and hyperemia fade in a few weeks, and the circulation usually returns to normal at this time.

Neuritic pain makes its appearance with partial recovery of the nerves and continues until nerve function is restored. It has disappeared within two weeks in some of the mild cases seen in Halifax, but it is impossible as yet to tell how long it may last in the severe ones. In some of the survivors observed in Scotland and in this series, it was troublesome for nearly six months.

Much can be accomplished by suitable treatment. This must be directed primarily at reducing local tissue metabolism in the early period and in preventing further injury and infection of the insensitive swollen feet. Gangrene should be a rare complication.

The rationale and methods of treatment developed so far are outlined, with suggestions for future investigation.

Not all cases of swollen painful feet seen in shipwrecked survivors are due to immersion in cold water. Cases in which this condition has developed in a tropical climate will be discussed in the second part of this paper.

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FIEDLER'S MYOCARDITIS*

Report of a Case

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NEW ORLEANS, LOUISIANA

SINCE Fiedler¹ first described interstitial myocarditis in 1900, there have been to our knowledge 9 reported cases of this entity in the American literature. Attention was first directed to this unusual form of myocarditis in the United States by Scott and Saphir.² In the world literature we were able to find at least 46 cases that conform to the pathologic criteria consistent with this syndrome.

Many quasi-descriptive terms have been used to identify the condition. Acute interstitial myocarditis was proposed by Fiedler. Later other synonyms were applied, and terms such as acute isolated interstitial myocarditis³; acute, subacute and chronic isolated myocarditis^{4,5}; myocarditis perniciosa⁶ and granulomatous myocarditis⁷ have appeared in reviews and case reports of this condition.

Because of the rarity of this syndrome, we believe that a brief survey of the literature and the report of an additional case are justified.

CASE REPORT

L. E., a 29-year-old housewife, was admitted to the Tulane Medical Service on October 21, 1939. She had been perfectly well until August of that year, when she experienced a sudden attack of "smothering" while doing her daily housework. At this time she was conscious of her heart's palpitating and was unable to get her breath. In a few minutes she was able to resume her work. Following this attack, she had occasional periods of dyspnea on exertion, which became progressively greater. Nine weeks prior to admission she began to experience attacks of paroxysmal nocturnal dyspnea. At about this time she began to require two to three pillows at night and

developed a cough productive of frothy sputum. Her activity was greatly restricted. Despite this the attacks of dyspnea became more frequent. On October 11, 1939, the patient was ordered to bed by her physician. At about this time she began to develop upper abdominal pain, noticed swelling of the upper abdomen, and began to vomit bile-stained material. Because of her failure to improve, the patient was referred to the Charity Hospital.

The past history was relevant in so far as it showed that the patient had had a cholecystectomy for cholecystitis and cholelithiasis 3 years previously. She had had "kidney trouble" and "high blood pressure" with a pregnancy 7 years previously. Subsequent follow-up over a period of years revealed no hypertension.

Physical examination disclosed an obese white woman who appeared to be of her stated age. The temperature was 100.4°F., the blood pressure 120/80, the respirations 30 and somewhat labored, and the pulse 108. There was enlargement of the right lobe of the thyroid gland, which was firm and smooth. Examination of the chest revealed lagging on the right side. The point of maximal cardiac impulse was felt in the 6th left interspace 8 cm. from the midsternal line. Tactile fremitus was diminished on the right posteriorly. There was dullness to percussion in this area below the 4th interspace. There was no enlargement of the heart to the right. The left border of cardiac dullness was 9 cm. from the sternal line in the 6th interspace. Breath sounds were heard with difficulty at the bases of the lungs, and vocal fremitus was greater on the left than on the right. Auscultation of the heart revealed no murmurs. The remainder of the physical examination was not noteworthy.

The red-cell count was 5,250,000, the hemoglobin 70 per cent, and the white-cell blood count 15,000, with a normal differential. The sedimentation rate was 20 mm. in 1 hour. Urinalysis was not significant, the specific gravity being reported as 1.022. The blood Wassermann reaction was negative. A roentgenogram of the chest was reported as showing enlargement of the cardiac shadow with evidence of pulmonary congestion. There was evidence of some fluid in the right pleural cavity.

The patient was digitalized, given oxygen by nasal catheter, and a thoracentesis of the right chest on October 22 yielded 1000 cc. of straw-colored fluid. Two days

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after admission a gallop rhythm and frequent ectopic beats were heard. A few days later the temperature rose to 100.2°F, and the patient ran an irregular fever for 9 days, *no cause other than pulmonary congestion being found.*

The basal metabolism was as follows: on November 8 the rate was +23 per cent, on November 10, +13 per cent, and on November 15, +3 per cent. Electrocardiogram made on October 23 revealed occasional ventricular premature beats and low, bizarre QRS complexes. T_2 was diphasic, and there was depression of the RST segment in Leads I and 2. The interpretation of the electrocardiographic evidence was extensive myocardial disease.

On November 25 the patient left the hospital against advice.

After leaving the hospital the patient felt quite well until June, 1940, when she began to decompensate. In the interval between June and November she was admitted to the hospital on two occasions. Her fourth admission occurred on November 25, 1940, when she returned at the request of the staff for further observation. At that time the blood pressure was 110/68. Investigation revealed that the heart had undergone progressive enlargement, particularly to the left. This was confirmed by roentgenologic examination.

On August 12, 1941, the patient was readmitted for the fifth time. She had been taking digitalis regularly up to 1 month before admission, when, on the advice of her physician, it was stopped for 14 days. In 2 weeks she developed dyspnea, palpitation and edema. Digitalis was resumed, but because of her heart failure she was advised to return to the hospital.

At the time of this readmission the temperature was 99°F, the pulse 90, and the blood pressure 130/80. Congestive rales could be heard at both bases up to the mid-lung fields. The heart border was percussed 4 cm. to the right of the sternal line and 13 cm. to the left of the midline in the 6th interspace. A gallop rhythm was heard. There were frequent ectopic beats and at times bigeminy was thought to be present. A pulse alternation of 10 mm. of mercury was noted. A systolic mitral murmur was heard. The liver was palpable three finger-breadths below the costal margin. Moderate edema of the feet, legs, sacrum and hips was present. The venous pressure was 24.8 cm., and the Decholin circulation time was 45 seconds. The patient was redigitalized and slowly improved, and early in September was allowed out of bed for short intervals. On September 21, she began to feel nauseated, vomited, and complained of abdominal pain. Because she was theoretically digitalized or perhaps overdigitalized, the drug was discontinued. She rapidly became worse, complained of dyspnea, and digitalis was resumed on September 24, with little effect. On September 28 the patient became extremely dyspneic and oxygen was ordered. She expired at 3:30 p.m. on September 29.

Autopsy. The outstanding pathologic changes were present in the heart, which weighed 450 gm. The epicardium was smooth and shiny, and the myocardium was relatively flabby. The coronaries were widely patent. In the region of the apex in the left ventricle there was a brownish, softened area that shrank beneath the cut surface and measured 0.8 cm. in diameter. In the inferior region of the left ventricle there was a firm, whitened scar penetrating a columna carnea that was approximately 1 cm. in length. The mitral valve had a number of wart-like protuberances, which appeared to be of the arteriosclerotic type. They were much larger than rheumatic lesions, being approximately 0.4 cm. in diameter. The

auricular endocardium above the mitral valve was thrown into threadlike folds and projections. Measurements were as follows: tricuspid valve, 130 cm; pulmonary valve, 74 cm; mitral valve, 107 cm; aortic valve, 60 cm; right ventricle, 05 cm, and left ventricle, 1.6 cm. The



FIGURE 1.

columnae carnea of the left ventricle were filled with grayish, apparently organized but easily removable thrombi. The other findings were pulmonary edema and congestion, chronic passive congestion of the liver and spleen and follicular cysts of the ovary. The thyroid gland showed no evidence of disease.

Microscopic examination of the heart revealed many areas of inflammation in the myocardium, varying in de-

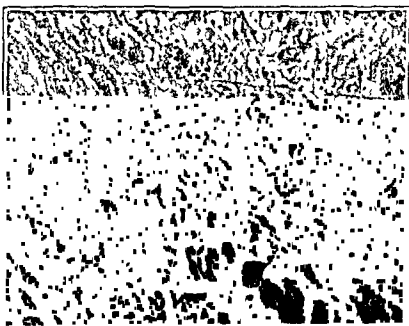


FIGURE 2.

gree and character. There was evidence of injury and repair of the muscle fibers associated with an infiltration consisting chiefly of lymphoid cells and an occasional polymorphonuclear leukocyte and phagocytic cell. Small areas of interstitial hemorrhage were present, but these were not remarkably prominent. There were areas where the degree of hydrops of the muscle was extreme (Fig. 1). At other sites an older lesion was demonstrable in which fibroblastic proliferation dominated the picture (Fig. 2).

DISCUSSION

The history and personal observations of the course of this case lead us to conclude that the disease began in June, 1939, and progressed to the patient's death in September, 1941. Search of the available literature on this subject discloses no other case of a patient with Fiedler's myocarditis surviving more than twenty-one months.

Many authors have attempted to incriminate definite etiologic factors that have been observed in connection with this disease. In the individual case reports carbuncles, gonorrheal urethritis, upper-respiratory infection, influenza, "rheumatism," syphilis and status thymicolymphaticus have been described as being associated in patients who have been found at necropsy to have interstitial myocarditis. Such an association is believed by most authorities to be coincidental and as yet no definite etiologic relations have been established.

Clinically no constant progression of symptoms and signs that is diagnostic of this pathologic entity is known. Its manifestations are protean. The reported cases show no preponderance of either sex. The disease occurs primarily between the ages of eighteen and fifty, although cases have been observed in patients as young as nineteen months^{8,9} and as old as sixty-nine years. The onset in the majority of cases is abrupt and may be accompanied by a chill. It may, however, be initiated by upper respiratory symptoms, such as cough, dyspnea, hemoptysis, generalized weakness and precordial distress.

Physical examination usually reveals no findings of any consequence. Some cases have presented evidences of focal infection of varying severity. There has been in some cases a slight but definite elevation of temperature for which no explanation was evident. In general the heart is enlarged, predominantly to the left, and at times a soft apical systolic murmur is heard. The rate is invariably accelerated, and a gallop rhythm has been described. There have been comparatively few electrocardiographic studies, but most of those reported presented evidence of definite myocardial damage. Despite this no diagnostic electrocardiographic criteria have been established for the condition.

The duration of the disease has been found to range from two days¹⁰ to twenty-one months.⁵ In

fact, one case is reported¹⁰ in which a patient died suddenly from a rupture of the left ventricle four days after a convulsive seizure. In the usual case, however, the disease will have run its course after a few months.

The histopathologic picture of this entity is characterized by typical findings.¹¹ There is usually an interstitial infiltration of the myocardium, which is chiefly due to lymphocytes, monocytes and, to a certain extent, neutrophils, eosinophils and plasma cells. Areas of necrosis are not infrequently found in the muscle fibers. This injury is diffuse throughout the myocardium. In some cases, hemorrhages have been described, due in all probability to the rupture of hyalinized muscle fibers. In the more chronic cases these areas are replaced by acellular fibrous scars. There may be actual granulation tissue with new capillary formation and fibroblastic proliferation.

Covey¹² emphasizes that no descriptions or illustrations contain all the abnormalities of the aggregate but that the variations pictured in the different case reports are insignificant when the whole is analyzed. It appears that whatever the etiologic agent may be, there is nothing in the histologic picture suggestive of a specific granuloma.

SUMMARY

A case of Fiedler's myocarditis is reported, and the significant clinical and pathological findings, as reported in the literature, are discussed.

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MEDICAL PROGRESS

RESPIRATORY FAILURE IN ACUTE POLIOMYELITIS

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THE increased interest in the treatment of acute poliomyelitis awakened by the Kenny technic has resulted in a certain amount of confusion regarding the value of the respirator in the presence of respiratory failure in this disease. The Kenny school of thought has gone so far in its condemnation of "orthodox practices" in this disease as to advocate the abandonment of the respirator in favor of the application of hot packs to respiratory muscles. This willingness to scrap the respirators along with the immobilizing splints calls for a review of the many complex factors involved in respiratory failure in acute poliomyelitis.

The muscles of respiration consist of two groups, one of which is engaged in quiet breathing known as eupnea; the other group, composed of the accessory muscles of respiration, comes into play during labored breathing or dyspnea. In the first group, there is a variation in the part played by the different muscles according to whether the subject uses the abdominal or costal type of respiration. In the dyspnea met with in the spinal type of poliomyelitis, the exaggeration of the breathing effort is manifested in those muscles that are attempting to compensate for muscles either weakened or completely thrown out of commission by spasm or paralysis. A muscle or a group of muscles that is in spasm may not be completely lost so far as potential function is concerned. In fact, muscles with an uninjured nerve supply may be thrown into continued contraction by the spasm of opposing muscles,¹ the so-called "brake" phenomenon in Kenny terminology.² Thus it is that the number of respiratory muscles thrown out of commission may be out of all proportion to the actual number of muscles or muscle fibers directly affected by nerve damage. This lost function is compensated for by the increased effort of the remaining, freely active muscles. This effort varies not only according to the amount of function lost but also according to which muscles are affected. There may be exaggerated abdominal breathing to compensate for loss of

function in the thoracic group, or exaggerated thoracic breathing to compensate for loss of function in the abdominal group. But as the demand for compensation increases, the accessory muscles of respiration come more and more into activity in an effort to lengthen and expand, as well as to contract, the thorax.

ANATOMY

The muscles engaged in forced inspiration are numerous. First of all is the diaphragm, which on contraction pulls air into the chest and simultaneously pushes out the abdominal wall. The thorax is also elongated by the upward pull of the three pairs of scaleni on the first and second ribs. The sternocleidomastoid and trapezius serve as accessories in this accordion process. Expansion of the thorax is accomplished by contraction of the levatores costarum, the external intercostals and the serratus posticus superior. By their action the ribs are raised and the shafts slightly rotated outward. In addition to all these we have the accessory action of the rhomboidei, pectoralis major and minor, serratus magnus, latissimus dorsi and, finally, the extensors of the spine.

Forced expiration is accomplished by contraction of the abdominal muscles, which, with the glottis open, forces the dome of the diaphragm upward and outward. Engaged in this process of shortening the thoracic cavity are the external oblique, internal oblique, transversalis and rectus, whereas the internal intercostals, triangulæ sterni, transversus thoracis and serratus posticus inferior tend to contract the thorax.

Although the function of some of these muscles is open to debate, they nevertheless all come into play in dyspnea. It is worthy of note that some one hundred and twenty separate muscles, as enumerated above, may go into vigorous action in forced respiration. Furthermore, it is clear that many of these, including the diaphragm, are far removed from any direct influence of hot packs. However, one can imagine that if the external intercostals were thrown into spasm and if the internal intercostals were to go into spasm by reflex action, both sets might be benefited by the application of hot packs to the chest wall. In this connection, it is a matter of clinical experience

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in poliomyelitis that the muscles of expiration show signs of serious fatigue sooner than do the muscles of inspiration. This coincides with the fact that even normal inspiration requires more muscular work than does expiration. The Drinker and the Emerson respirators, by creating rhythmic negative pressure, take over the work of the inspiratory muscles. The pulsator of Bragg and Paul, on the other hand, rhythmically compresses the chest wall by pressure from a rubber bag fastened about the chest. This compression takes the place of the expiratory muscles in forced expiration, as in the Schaefer method of resuscitation. Of the two, the respirator much more closely imitates normal respiration.

PHYSIOLOGY

The respiratory center in the medulla or bulb lies under the floor of the fourth ventricle in the region where the cranial nerves originate. This center has a right and a left half, which communicate with one another through the intrabulbar commissural fibers, giving a symmetry of respiratory movements. The main function of this center is to regulate the rhythm and the depth of the involuntary respiratory movements. It does this through afferent impulses arising from various sources which convey the body needs. From here also fibers pass directly downward without decussation to the respiratory motor nuclei in the anterior horns of the cord. Any impairment of this respiratory center in the medulla results in variations in rhythm and depth, and its destruction results in immediate cessation of respiration.

This respiratory center is in anatomic and physiologic relation to certain cranial nerves whose afferent fibers bring controlling impulses of inspiration and expiration. The most important of these is the vagus, the sensory fibers of which come from the lungs, bronchi, trachea and larynx, whereas the motor fibers supply these same areas, together with the pharynx and soft palate. These impulses exert essential influences for both the rate and the rhythm of involuntary respiration, and also for the more violent voluntary efforts of coughing.

Sensory fibers of the trigeminal nerve arising from the nasal mucous membrane have an important protective function. Any violent irritation of these nerve terminals by injurious gases inhibits breathing. The same effect is obtained from any marked irritation of the glossopharyngeal nerve. In fact, the sensory fibers of this nerve inhibit respiration whenever one swallows.

Involuntary respiration is under the control of the respiratory center in the bulb. Voluntary control comes from the cerebrum, as in talking, singing, whistling and any blowing effort. But there

are impulses that involuntarily interrupt the normal rhythm, such as yawning, laughing, sighing, crying and sobbing. Coughing and sneezing arise from irritation along the tract. Hiccup, a spasm of the diaphragm with closure of the glottis in the form of an extra inspiratory wave, can be induced by a wide variety of causes including irritation of the diaphragm, intoxication, encephalitis, irritation in the trapezius³ and exsanguination in its terminal stage. Of these all but the last may occur in poliomyelitis. The hiccup in this disease is a subject that in itself deserves extensive discussion.

SPINAL RESPIRATORY FAILURE

When a healthy individual is placed in a respirator, his respiratory rhythm is promptly taken over by the machine without his becoming aware of it until he tries to talk. He can articulate only with each expiration. He finds himself merely making motions of the tongue and lips during inspiration, and he cannot prolong expiration against the machine. A patient in the respirator learns very promptly—within a few minutes—how to talk and how to swallow nourishment, if minute amounts are given at first. He does not have to be taught by anyone: it is a matter of extraordinarily prompt adaptation to an artificial respiration that closely simulates normal breathing.

The respiratory center serves as the pacemaker for a wave of musculature contraction starting in the diaphragm and co-ordinately bringing into play those muscles of the thorax and abdomen that are needed. The diaphragm may "flutter" in post-encephalitic conditions and, in so doing, may carry the thoracic muscles along at the rate of 90 or even 200 contractions a minute, a very uneconomical form of respiration, with movement of air largely confined to the "dead spaces," and with very little change of air in the lung itself. Dowman⁴ and Skillern⁵ have shown that under these conditions, when the diaphragm is put out of commission by a double phrenectomy, the other respiratory muscles promptly return to a contraction rate of 20 per minute. Gamble, Pepper and Muller⁶ observed that occasionally in flutter the chest muscles would "miss" and, further, that immediately after prolonged holding of the breath or during sleep the diaphragmatic flutter would at times fall into an exact two-to-one rhythm with the thoracic excursions.

All this puts one in mind of the relation of the auricles to the ventricles in cardiac rhythm, an analogy discussed by Wenckebach.⁷ But there is a wide difference between the respiratory and the cardiac systems, since there is no pacemaker in the diaphragm and no "conduction system" other than the nerve supply from the respiratory center to the

respiratory muscles with the synapses in the spinal cord. Nevertheless, the co-ordination in the wave of contractions and the disturbances in rhythm offer an interesting comparison from a clinical viewpoint. An appreciation of these outward similarities helps one to recognize some of the respiratory phenomena observed in poliomyelitis.

In spinal poliomyelitis only one side of the diaphragm may be thrown out of commission.⁸ One may observe a patient getting along fairly satisfactorily with apparently a complete unilateral absence of contractions. Likewise a patient will sometimes appear to be getting along well with only the diaphragm and very little use of either the thoracic or the abdominal muscles. However, these patients should always be in close proximity to a respirator, and be put in at the first sign of fatigue. Although a patient may seem to be getting enough air under these conditions, he will often get relaxation and comfort in the respirator so that he promptly falls asleep.

Indications of impending failure in the spinal type of poliomyelitis consist of visible loss of action in the muscles of normal inspiration, with overaction of the sternocleidomastoid ("neck breathing") and other accessory muscles. The breathing is at first shallow and later labored. Speech is interrupted by inspirations so that the patient can count only to two or three before breathing in. Coughing becomes ineffective and then impossible. Cyanosis implies anoxemia, with lowered resistance to the infection as a whole, as well as loss of muscle strength. When all inspiratory effort is apparently on the point of exhaustion and the expiratory muscles appear to be attempting to compensate with a low vital capacity of air in the lungs, the need of a respirator is imperative. The ideal time to put the patient in is at the first signs of failure. Delay is to his distinct disadvantage.

The supportive value of the respirator when early fatigue is threatened is difficult to determine in statistics, yet it may be quite obvious to the patient and to the attending clinician. Nor does such a statement preclude the use of hot packs as an intermediate measure. Indeed, I have seen hot packs enhance the inspiratory effort of the thoracic muscles when these were lagging, but such benefit was temporary. One may assume that muscular spasm is relaxed by the heat, but certainly the heat does not reach a diaphragm in spasm. Whether the respirator has a salutary or detrimental influence on any of the respiratory muscles in spasm is unknown. At least, one can say that there is no danger of muscle-stretching. Short of complete paralysis there is certainly no rest for these muscles, in the true sense of the term, while life goes on. The respirator may secure rest to some of the over-

worked accessory muscles, but primarily it serves as a support to the muscles of normal quiet inspiration.

As pointed out by Wilson,⁹ the nearest approach to achieving rest for the respiratory muscles comes from the proper use of a respirator. This machine is to failure of the respiratory muscles what intubation is to laryngeal obstruction. In this comparison the preliminary trial of hot packs may be compared to the use of steam inhalations in laryngeal spasm. There are definite indications for the respirator as there are for intubation. Delay in the use of the respirator as with the tube results in fatigue and anoxemia, and may mean the difference between death and recovery. Just as the tube should not remain in any longer than is necessary, so also the patient should be weaned from the respirator as soon as possible. Ability to cough is a good indication for removal.¹⁰ The respiratory muscles can be "alienated" from the control of the respiratory center as definitely as the leg muscles can be "alienated" from the cortex by prolonged immobilization in a splint.

In complete and irreversible paralysis of the respiratory muscles, life can be maintained only by the continued use of the respirator. However, as pointed out by Wilson,¹¹ there is no way of telling at the beginning of muscular failure how much nerve damage is actually taking place. Nor, as he says, is there any room for philosophical discussion of one's duty as a physician even if one could foresee indefinite dependence on the respirator. Furthermore, the established fact that there is a high death rate from respiratory infections following the use of the respirator is also no argument against its use, since this also holds true after intubation and tracheotomy. Indeed, the utmost care should be used in respirator cases to avoid exposure to respiratory infections. All attendants should wear masks, and no visitor with a cold or sore throat should ever be allowed in the room.

The rate of the machine is not so important as the height of negative pressure. In the pure spinal type the patient's respiratory rate depends on the degree of failure, but once in the apparatus he promptly adapts himself to its rate. This is particularly shown in the room respirator where several patients are being treated at the same time.¹² The rate for children is usually between 20 and 30 per minute, and for adults between 15 and 20 per minute. The pressure, however, is a very different thing. The real danger of the machine lies here. Too great a negative pressure injures the alveoli of the lungs and thereby induces pneumonia.¹⁰ Children under ten years of age should be started at a pressure of 10-cm. on the water manometer, and this should never be to

rise above 14. Adults can be started at a pressure of 12 to 14 cm., and there is rarely any reason for allowing it to rise above 16, and never above 20. The four most important points to keep in mind in the use of the respirator in the spinal type of failure are these: avoid delay; wean as early as possible; avoid dangerously high negative pressure; prevent bedsores. The nursing care of respirator cases is described in a brochure put out by the National Foundation for Infantile Paralysis.¹³

BULBAR RESPIRATORY FAILURE

Respiratory paralysis in poliomyelitis is not confined to impairment of the respiratory muscles through injury to their spinal-nerve supply. The virus may attack other portions of the nervous system whereby respiration is affected, either directly at the respiratory center itself, or indirectly through injury to those cranial nerves supplying certain muscles that clear the respiratory tract by swallowing.

When the respiratory center itself becomes impaired, the respiration becomes irregular and jerky. This irregularity is not overcome by the respirator. In other words, the respiratory movements fail to synchronize with the machine. Along with this there may be long sighs or violent hiccups that add to the confusion of the breathing. In a way this may be compared to the twitching and fibrillation seen in the trapezius muscle when its anterior-horn cells are being invaded by the virus. Suddenly and without further warning respiration stops. On the other hand, one may see a marked slowing of the rate with deep inspirations, signifying pressure on the floor of the fourth ventricle from increased spinal-fluid pressure. Lumbar drainage promptly performed can offset such a situation, and with repetitions as needed may lead to the return of normal respirations as the pressure subsides.¹⁴

The function of deglutition is vital to respiration, as this keeps the upper respiratory tract clear. Any impairment of this function through injury to the cranial nerves supplying this area results in choking and finally drowning in mucus. This is the so-called "wet type" of respiratory failure. To speak of these patients as dying of pneumonia is misleading. Of course, they may do so later from a secondary infection. In these cases with inability to swallow the respirations are shallow and often irregular, because the patient hesitates to breathe for fear of inspirating mucus into the trachea.¹⁵ With laryngeal paralysis coughing becomes impaired because of an inability to close the glottis. Thus it becomes impossible to clear the throat by either swallowing or coughing. The accumulation of mucus tickles the underlying

mucous membrane, with the result that the secretion of mucus is rapidly augmented. Nausea may be an additional factor in the promotion of excessive mucus. It is possible that the invasion of the pharynx by the virus of poliomyelitis in these cases may also be another factor in this profuse secretion of mucus. The recent work of Sabin¹⁶ indicates that bulbar invasion originates from extension of the virus along the neurons supplying the pharynx, whereas spinal involvement originates from extension of the virus along the neurons supplying the intestine.

Landon and Smith,¹⁷ Kelleher¹⁸ and Emil Smith¹⁹ state that atropine is useful in drying up these secretions. Crone¹⁹ remarks that atropine gives only temporary and partial relief. Wilson²⁰ has found it unsatisfactory and believes that it may render the mucus more tenacious, more annoying to the patient and more difficult to remove. My own experience is that, although atropine is oftener useless than helpful, it has at times appeared to slow up the secretions perceptibly.

Suction applied to the pharynx is a great help, but it must be exerted very gently. Anderson²¹ uses a rubber catheter with numerous openings near the tip. This is passed through one nostril down into the pharynx and constant suction is applied. With sufficient skill a tube may be passed through the other nostril and down through the esophagus to the stomach for the purpose of feeding. Needless to say, one must be sure that this tube lies in the stomach. The foot of the bed is raised sufficiently to give the trachea enough of a downward slant to procure gravity drainage.

Postural drainage is of far greater importance than either atropine or suction, as has been graphically brought out by the cases reported by Durand.²² With the foot of the bed raised 2 feet enormous quantities of this mucus—a pint or more—will run from the nose and mouth in spite of the administration of atropine. The patient's position can be shifted from one side to the other—better still with the face down but turned to the side.

The respirator is not only useless for correcting the embarrassment to respiration in bulbar poliomyelitis, but can be actually harmful. As has already been said, when the respiratory center is involved the patient's breathing does not synchronize with the machine. Thus the machine interferes with his breathing instead of supporting it, and he begs to be taken out. When cranial-nerve involvement causes pharyngeal paralysis, the respirator causes the mucus to be forcibly drawn down into the trachea, whereas the patient's own intuition prompts him to avoid this by shallow breathing. Nevertheless, it must be clearly

understood that a patient may have a combination of spinal and bulbar involvement, and the spinal involvement may be sufficiently severe to warrant a trial of the respirator, provided precautions are taken against the effects of the bulbar paralysis. Especially is this true where the spinal involvement is severe and the bulbar involvement is mild. When pharyngeal paralysis is combined with the spinal type, an inlaid catheter with constant suction can be tried along with the respirator. To meet this combination of circumstances a respirator is now available that can be adjusted like an operating table and thus afford postural drainage as well. However, the mortality rate in these cases is always high, especially in those with the ascending type of paralysis.

* * *

There is one condition that occurs, especially in the ascending type of spinal paralysis, where the respirator becomes useless. The abdominal muscles become paralyzed first, as their nerve supply comes from the dorsal segments of the cord. Next, the thoracic muscles cease to function, their nerve supply coming from the cervical segments. If the diaphragm, which is also supplied by the cervical segments, holds out long enough to get the patient to a respirator, dramatic and immediate relief may be obtained. But unfortunately, the paralysis of the intestinal tract then begins to manifest itself with absolute stasis and increasing abdominal distention. Hot stupes, enemas and the rectal tube become ineffectual. A Miller-Abbott tube cannot be worked down beyond the pylorus under these conditions. The weakened and eventually paralyzed diaphragm is forced higher and higher. Finally the negative pressure of the respirator, even when increased to 30 cm. on the water manometer, fails to enlarge this contracted thoracic cage. A respiratory standstill may thus ensue in spite of the respirator before the medulla is encroached on.

Condemnation of the respirator by the close adherents of the Kenny method has been uttered from the lecture platform. I witnessed this in the crowded Kenny booth at the last meeting of the American Medical Association in Atlantic City, and again at the course given at the University of Minnesota last July, where the lecture and motion picture dealing with respiratory paralysis were unforgivably narrow in scope and in tone. This exercise was not conducted by Sister Kenny. In her book Sister Kenny² describes the success of her treatment in two early "respirator cases" in which the patients were "unable to swallow," and in a spinal case where artificial respiration by "gently depressing the floating ribs" was

resorted to five days after the onset of the poliomyelitis. She describes it as a form of "muscle education"—that is, teaching the patient to breathe. That Sister Kenny inspires confidence in her patients and overcomes their fears is one of her great assets. But one is also impressed by her outspoken prejudice against all orthodox treatment. Thus, she prefers the old method of resuscitation that all physicians had to use before the invention of the respirator. A careful analysis of the respiratory cases treated by Daly and her associates²³ by the Kenny method is not at all impressive in this particular respect, although otherwise it is highly instructive. Enthusiasm for the Kenny technic has led many to accept it as an all-embracing system of treatment for poliomyelitis. Such an attitude is out of keeping with the professed philosophy of Sister Kenny herself at her highest moments as a teacher. Hot packs to the chest, neck and abdomen may be advantageously applied in the earliest stage prior to insertion in the respirator and on removal from it, or where no respirator is available.

The use of the respirator is fraught with many discouraging experiences. Some are due to the types and complications of the respiratory failure, but others result from the overwhelming damage brought about by the progress of the disease. These experiences have been stressed by all authors, and powerfully expressed in an editorial.²⁴ Nevertheless, on the credit side there are an ample number of patients who have obtained comfort, relaxation and sleep at a critical period of respiratory embarrassment, and who later have walked out of the hospital to lead useful lives. It is impossible to draw up an adequate protocol of the results of respirator treatment over the last decade, because of the relatively small number of publications on this subject. However, in a survey of the year 1940 Wilson²⁴ found that among 127 cases with simple intercostal or diaphragmatic paralysis treated in the respirator, 81 per cent survived. The survey could not include the end-results regarding permanent handicaps. It did bring out that in general the respirator was too frequently used where it was not indicated, and that where indicated its use had too often been delayed to the distinct disadvantage of the patient. Unqualified disparaging statements regarding the value of the respirator increase these delays. The Kenny method has much in its favor, but as yet no figures have been produced to show that hot packs can replace the position now held by the respirator in the treatment of the spinal type of respiratory failure in poliomyelitis.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29071

PRESENTATION OF CASE

A sixty-five-year-old woman entered the hospital because of "gas around the heart" and palpitation.

Approximately one year before entry the patient developed slight constipation, which was relieved readily with mineral oil or milk of magnesia. Since that time she had had intermittent attacks, that is, two or three times per month, of periumbilical crampy pain, each lasting several hours. These were unrelated to food intake or activity and were sufficiently severe on only one occasion to force her to bed. She had had no recurrence of this pain during the four or five weeks prior to admission. She attributed this to pills prescribed by her physician. However, five weeks before entry she began to suffer with considerable belching and sour eructations. The belching was worse at night and half an hour after meals, but was not otherwise related to activity and was not effected by bowel movements. During this same period, palpitation frequently occurred at night. At no time had there been malaise, anorexia, nausea, vomiting, diarrhea, melena, jaundice, dyspnea, orthopnea or ankle edema.

The family and past histories were noncontributory.

Physical examination revealed a moderately obese, somewhat apprehensive woman who did not appear to be uncomfortable. The chest was barrel shaped. Examination of the lungs was negative. The heart was considered enlarged to the left; the sounds were of good quality and no murmurs were audible. The abdomen was soft. There was slight tenderness and a poorly defined mass in the left lower quadrant.

The blood pressure was 167 systolic, 90 diastolic. The temperature was 97.6°F., the pulse 88, and the respirations 18.

The examination of the blood revealed a hemoglobin of 14.7 gm. and a white-cell count of 9700 with 69 per cent polymorphonuclear leukocytes. The urine was normal except for a rare white and epithelial cell in the sediment. A gas-tic analysis revealed no free acid in the first

specimen and 15 units in the specimen collected an hour later. The gastric contents were guaiac negative. Repeated stool examinations were guaiac negative. A Graham test was negative. A barium enema showed narrowing and marked mucosal swelling of the midportion of the sigmoid over a distance of approximately 10 cm. Definite ulceration of the mucosa was not visible. There were numerous diverticula in the sigmoid and descending colon. The colon proximal to the lesion was not examined. Ten days later the barium studies were repeated, barium being introduced by means of a Foley catheter. At this examination there was complete obstruction in the sigmoid in the area of greatest narrowing previously described. The exact nature of the lesion could not be demonstrated because insufficient barium passed the point of obstruction.

An operation was performed on the sixteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. REGINALD M. SMITHWICK: The history indicates that this sixty-five-year-old woman had had symptoms referable to the gastrointestinal tract for about a year. One of these was slight constipation, which apparently did not increase in severity and was easily relieved by nondrastic laxatives. There were also short periods of crampy abdominal pain occasionally lasting several hours. Later, belching and sour eructations but no nausea or vomiting were noted. There was no distention, increased peristalsis or fever. An indefinite, slightly tender mass in the left lower quadrant tends to incriminate the large intestine. This was confirmed by a barium enema, which revealed a process involving the midportion of the sigmoid—with marked narrowing on the first examination and complete obstruction on a second examination ten days later. There is no evidence in the history of other clinical signs of complete obstruction, such as distention, pain, increased peristalsis, nausea and vomiting. Apparently her bowels moved in spite of the x-ray evidence of marked obstruction, since it is reported that repeated stool examinations were negative for occult blood.

The question for discussion seems to be the nature of the lesion in the sigmoid colon. The x-ray suggests an intrinsic process. A review of the films may be helpful.

DR. GEORGE W. HOLMES: There is nothing of interest in the chest. The gall bladder is well seen and looks normal. The colon is obviously abnormal, and the picture is characteristic of diverticulosis, with multiple large diverticula scattered throughout the descending colon and sigmoid.

At one examination there was no definite obstruction. At another examination ten days later there was definite obstruction. At the first examination, in addition to the diverticulums, there was evidence of spasm. The film taken in the lateral view shows a good outline of the lumen of the large bowel, and it does not seem possible that a tumor large enough to plug the bowel could have been present and have been completely missed at this first examination. At the second examination the filling is insufficient and one could miss a tumor, but I should not expect a large tumor to appear in such a short interval. So far as the x-ray demonstration goes there was no ulcerated lesion or tumor, so our interpretation would be that the obstruction was due to the diverticulitis.

DR. SMITHWICK: The two most likely diagnoses are carcinoma and diverticulitis, with or without a localized perforation and abscess. It is possible that both lesions were present. These seem more probable explanations for the sigmoid lesion than tuberculosis, lymphoma, endometriosis, metastatic carcinoma or the extension of a primary lesion of the left uterine adnexa to the bowel. There is no evidence of a benign polypoid tumor of the bowel.

With regard to the differential diagnosis between cancer and diverticulitis, it is at times easy, at times difficult, and occasionally impossible. The age of the patient is not helpful, since either lesion is probable at sixty-five; and the duration of symptoms is quite in keeping with either diagnosis. The absence of clinical symptoms of increasing constipation favors a diagnosis of diverticulitis, whereas the x-ray evidence of complete obstruction leads one to favor cancer, particularly if it persisted after a few weeks of proximal decompression of the bowel. The location of the lesion—the sigmoid area—is a characteristic one for both carcinoma and diverticulitis. The absence of blood in the stools is definitely in favor of diverticulitis, since bleeding is present in only about 16 per cent of the cases of diverticulitis and usually occurs in cases of cancer. The presence of a mass is not helpful. Even at operation one often cannot differentiate the two lesions by inspection or palpation. The pathologist has to decide the matter following resection of the involved area. The x-ray evidence obtained from the first barium enema favors diverticulitis because of the long segment involved (10 cm.) and the absence of destruction of the mucosa. The presence of both lesions is statistically unlikely, as diverticulums have been found associated with carcinoma in only 0.6 per cent of cases, whereas cancer has been found associated with diverticulitis in only 1.8 per cent of cases.

It seems to me that the evidence at hand favors a diagnosis of diverticulitis of the sigmoid with a recent increase in the inflammatory process; an associated localized perforation is a reasonable explanation for the recent x-ray evidence of complete obstruction.

DR. TRACY B. MALLORY: If you had a choice between the two alternatives, Dr. Holmes, which would you choose from the x-ray point of view?

DR. HOLMES: There is no x-ray evidence of tumor. If we made the diagnosis from the x-ray examination alone we should have to say diverticulitis.

CLINICAL DIAGNOSIS

Diverticulitis.

DR. SMITHWICK'S DIAGNOSIS

Diverticulitis of sigmoid.

ANATOMICAL DIAGNOSES

Carcinoma of sigmoid.

Diverticulosis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was operated on and a segment of the sigmoid was found to contain many large and deep diverticulums. The involved segment was moderately firm. The surgeon's preoperative diagnosis was diverticulitis. When he finished the operation he apparently wavered a bit, since he raised the question of carcinoma; but he still put down diverticulitis as his first diagnosis.

When the sigmoid was opened in the laboratory, a small annular cancer was found in the midst of the segment, which had caused a significant grade of obstruction. We could find no evidence that any of the diverticulums were inflamed, and we thought that they were purely coincidental and that the symptoms were due to carcinoma.

DR. SMITHWICK: How do you explain the difference in the barium enema in ten days?

DR. MALLORY: There might have been enough difference in the pressures used during the two examinations.

DR. HOLMES: So one got through and the other did not? I hardly think so. Where was the cancer?

DR. MALLORY: In the midst of the area of diverticulosis in the sigmoid.

DR. HOLMES: At the second examination the obstruction does not seem to be abrupt, and I wonder if they failed to get the enema in.

CASE 29072

PRESENTATION OF CASE

A thirty-three-year-old man was admitted because of nausea, vomiting, stiff neck and headaches.

Three weeks prior to admission he developed a stiff neck. This was followed ten days later by the onset of severe headaches and then by nausea and vomiting. He soon began to vomit continuously, and was unable to retain anything so that during the week prior to admission he had had no fluids or solids by mouth. Five days before entry he entered a community hospital, where he was found to be afebrile and weak. He became drowsy and lapsed into coma. He was treated with intravenous fluids. A lumbar puncture revealed an initial pressure of 235 mm. of water, and after removing 10 cc. of clear fluid, the pressure was 100 mm.; there were 3 cells per cubic millimeter. Examination of the blood showed a white-cell count of 9200, a red-cell count of 4,000,000 and a hemoglobin of 76 per cent. The coma persisted until the evening prior to admission to this hospital.

The patient was known to have Huntington's chorea, as did his mother and maternal grandmother. For a number of years he had had involuntary twitches and sudden movements of both arms. He was able to sit quietly, but staggered drunkenly when he walked; he had recently had urinary incontinence. Thirteen years before entry, following a blow to the back of the head, he was said to have suffered concussion. Eight years later he injured his head but was not rendered unconscious. He frequently bumped his head and injured himself.

Physical examination revealed a well-developed, dehydrated semicomatose man lying in bed with his neck hyperextended and stiff, and breathing slowly and deeply through the mouth. The tongue and mucous membranes of the mouth were dry, crusted and caked. The right eye blinked continuously. Both eyes were held with the gaze upward and to the right, although the patient was able to move them voluntarily. The fundi were normal. Examination of the heart was negative. There was dullness with absent breath sounds at the right lung base posteriorly, and a few moist rales were audible at the left base posteriorly. No masses were felt in the abdomen. There was a continuous tremor of the left forearm and the fist was tightly clenched. The tendon reflexes were active. The abdominal and cremasteric reflexes were absent. The Babinski reflex was positive on the right. No clonus could be demonstrated.

The blood pressure was 110 systolic, 80 diastolic. The temperature was 101°F., the pulse 100, and the respirations 25.

The examination of the blood revealed a red-cell count of 5,570,000 with a hemoglobin of 14.6 gm. and a white-cell count of 18,250 with 90 per cent polymorphonuclear leukocytes. The urine was acid in reaction, had a specific gravity of 1.030 and gave a ++ test for albumin; the sediment contained innumerable red and white cells. The urine was unchanged when examined on the succeeding two days. The blood Hinton test was negative. A blood culture revealed no growth. The blood nonprotein nitrogen was 34 mg. per 100 cc., the chloride 115.8 milliequiv. per liter, the total protein 6.8 gm. per 100 cc., the calcium 10.8 mg., and the phosphorus 4.0 mg. A lumbar puncture showed an initial pressure of 110 mm. of water; no cells were found in the spinal fluid, and the gold-sol curve was normal; the protein was 27 mg. per 100 cc. The spinal-fluid Wassermann test was negative. An x-ray film of the chest demonstrated a mottled consolidation in the right lower lung field; there were old scars in the right apex.

The patient was treated with parenteral fluids, and a total of 5 gm. of sodium sulfadiazine was administered intravenously on two days without noteworthy effect. The blood sulfadiazine level on the third hospital day was 4.1 mg. per 100 cc.; the bicarbonate was 25.6 milliequiv. and the chloride 107.7 milliequiv. per liter, and the nonprotein nitrogen was 26 mg. per 100 cc. The patient died on the fourth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. MANDEL E. COHEN: To summarize this history briefly, the patient was a young adult who had Huntington's chorea, and it is said that his family had the same trouble. Twenty-one days before admission he had a stiff neck. Ten days before, he had nausea, headache and vomiting and could take nothing by mouth. Five days before, he became drowsy, lapsed into stupor, then coma and apparently when admitted to this hospital was comatose, in fact, we may say he was moribund.

Did the patient have Huntington's chorea, or was that an erroneous diagnosis? All we can do is accept the diagnosis, as it is a well-known syndrome and was present in the patient's family. He was a bit young to have it so far developed, but that is quite all right.

The next question is, Is the incident which led to the patient's death one that is explained by Huntington's chorea, and was it the natural

development of the illness? The answer to that I should say is, No. Patients with uncomplicated Huntington's chorea do not develop sudden acute changes in the central nervous system that cause headache, stiff neck, vomiting and so forth. So I think we shall have to postulate that some other disorder complicating the Huntington's chorea led to the patient's illness and death.

Does the fact that the patient had Huntington's chorea in any way alter the history and the examination? I should say that that certainly is a possibility, because if this man had considerable cerebral change, with psychologic symptoms, it would have been difficult to obtain an accurate history either from him or from his family. Furthermore, the patient probably first consulted his physician late in his illness. There are two other consequences of Huntington's chorea that should be mentioned in connection with this case: one is trauma, and the other is suicide. These patients frequently fall down. A case is recorded in which a man suddenly spun around and fell into a plate-glass window. Another patient, standing near a flight of stairs, had one of the jerky movements of Huntington's chorea, fell over backward and was killed. Suicide is of high incidence in this group, and the question might be raised whether this man had taken some poison, such as bichloride of mercury. We have no evidence for that, but I think we must keep the possibility of trauma in mind, particularly since we are told that he had hurt himself in the past.

I shall assume that some intracranial difficulty led to the patient's final illness and death and that it was a fairly acute process—not something that came as a natural development of Huntington's chorea. There are two good possibilities: one is neoplasm, and the other is subdural hematoma.

In addition we should consider the other types of disease that commonly occur in the brain. First, did the patient have a vascular lesion? Against that are his age and the slow onset. Furthermore, he had no other evidence of vascular disease—no high blood pressure or blood in the spinal fluid. Did he have an infectious lesion in the brain? Here again we do not have evidence for that sort of diagnosis. There was no obvious primary focus of infection. The record states nothing about the ears or sinuses, but I shall assume that they were examined and were normal. He did have a pulmonary lesion, which was detected when he was here but not at the first hospital. Without any further information, I must interpret that as a terminal bronchopneumonia. Against infection are the facts that he was afebrile, that the white-cell count was normal and that the spinal fluid on two occasions showed no cells or elevated protein.

I suppose he could, as a remote possibility, have had a brain abscess, but we have no evidence in that direction. Hence, infection was probably not the cause of this man's difficulty.

So that still leaves us with the two possibilities previously mentioned. He probably had a mass of some kind, either a tumor or a subdural hematoma. There is not enough evidence to localize the lesion accurately. Two localizations fit some of the facts, but neither fits all of them. One is that the mass was in the posterior fossa. In favor of that is the fact that the patient had a stiff neck, headache and abnormalities of head posture and eye movements; against it is the fact that the intracranial pressure was not particularly elevated, since the optic disks were not choked. There is some evidence for a more anterior lesion, such as one in the left cerebrum, since the right eye blinked continuously. He had a positive Babinski sign on the right side and tremors on the left—not on the right. One might say that the tremors were due to the chorea and the left-sided lesion had stopped the tremors, but that is just speculation.

I should say that in treating this patient burr holes should be made for a subdural hematoma and that if this were not found a tumor should be looked for. But in making the diagnosis I should place neoplasm first and subdural hematoma second.

If this was a tumor, was it primary or secondary? Metastasis might have occurred from a tumor of the lung. We do not know whether the lesion at the right lower base was due to pneumonia or whether there was some evidence of tumor. In addition, we have not explained satisfactorily the red cells in the urine. Did he have a bladder tumor, which would also account for the incontinence? If we can believe the history, the illness started out of a clear sky with a stiff neck; the red cells were probably due to catheterization on several occasions.

At autopsy, we shall probably be told that in the brain there were the changes characteristic of Huntington's chorea, with atrophy of the cortex and of the caudate nuclei, together with a primary neoplasm, possibly a glioma, which I cannot localize or with a subdural hematoma, and with bronchopneumonia and cystitis.

DR. AUGUSTUS ROSE: The importance of a stiff neck in pointing to infection of the central nervous system is worth discussion. Dr. Cohen has assumed that it does not necessarily indicate infection. I should like to ask Dr. Cohen to discuss the mechanism of stiff neck in posterior-fossa tumors.

DR. COHEN: I do not know, and there is no final evidence in the literature. I suppose the general explanation is that such a stiff neck means irritation of the tentorium, which in turn causes the extensor reflexes of the neck to be stimulated; this can occur either with a lesion in the posterior fossa or with a mass in the brain that acts by pressure or herniation.

DR. ROSE: Do you consider this a kind of decerebration?

DR. COHEN: Yes.

CLINICAL DIAGNOSES

Huntington's chorea.

Bronchopneumonia.

Encephalitis?

DR. COHEN'S DIAGNOSES

Huntington's chorea.

Brain tumor (? glioma) or subdural hematoma.

Bronchopneumonia.

Cystitis.

ANATOMICAL DIAGNOSES

(Huntington's chorea.)

Subdural hematomas, bilateral, massive.

Bronchopneumonia, confluent, right lower lobe.

Cystitis, acute hemorrhagic, marked.

PATHOLOGICAL DISCUSSION

DR. CHARLES S. KUBIK: There was a large subdural hematoma on each side, the one on the left

being the larger. Since the membranes surrounding the hematomas were fairly dense, the lesions were probably several months old. There was a large temporal pressure cone on the left side, and a smaller one on the right, with resulting compression of the midbrain and aqueduct. There were hemorrhages in the midbrain, a common finding with a temporal pressure cone. Compression of the midbrain and aqueduct probably caused an actual dynamic block, which accounted for the low spinal fluid pressure (110 mm.). Removal of fluid by lumbar puncture would have a tendency to make a bad situation worse by allowing the pressure cone to herniate farther. Pressure against the midbrain or stretching of the tentorium or both may also have had something to do with the stiffness of the neck.

Other changes, presumably related to the Huntington's chorea, were marked atrophy of the caudate nuclei, diminution in the size of the lenticular nuclei and enlargement of the lateral and third ventricles.

Flattening of the cortex by the hematomas made it difficult to estimate the degree of cortical atrophy.

DR. TRACY B. MALLORY: There was a well-marked cystitis, which was certainly the cause of the red cells in the urine and probably the result of catheterization. The lungs showed diffuse congestion and edema, with an area of bronchopneumonia at one base.

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THE VICISSITUDES OF WAR

For the duration of the war the *Journal* has been obliged to adopt changes that are not of its own choosing. Paper is becoming scarce and all publishers of periodicals who buy more than a certain tonnage each quarter have been limited by the War Production Board to 90 per cent of the paper used in 1942. Furthermore, owing to the need for chlorine in the manufacture of munitions and other war materials, the good grades of paper pulp are unobtainable. In addition, the scarcity of manpower is a distinct handicap to the typesetter, the printer, the binder and the mailer. And, finally, the entrance of so many physicians in and around

Boston into the armed forces, particularly young men, who are apt to be engaged in clinical or experimental investigative work, has resulted in a marked reduction in the number of contributors to the *Journal*; whereas those who remain at home, for one reason or another, are so deluged with extra duties that the writing of a paper, which to almost everyone is a chore, is necessarily, and probably thankfully, put aside. A reasonable number of papers are still being submitted for publication, but the members of the editorial board are unanimous in their belief that quality should not be sacrificed for quantity—in other words, that the high standards for acceptance should not be lowered.

In the future, the readers of the *Journal* must be content with receiving, somewhat tardily, a periodical of smaller size and one that is printed on a poorer grade of paper. It is anticipated that the two weekly features, "Medical Progress" and the "Case Records of the Massachusetts General Hospital," can be continued, but original articles, like sugar and coffee, must be rationed. For all this, the *Journal* apologizes, but asks that its subscribers accept these unavoidable changes with the same spirit that they have shown regarding the many real sacrifices entailed by the war effort.

PROPHYLACTIC SULFONAMIDE THERAPY

MECHANIZED warfare and rapidly changing areas of combat often preclude immediate definitive surgical care of war wounds and burns. Various combinations of general and local sulfonamide therapy have been suggested as part of the first-aid routine to delay or prevent the onset of infection during the period of evacuation to competent surgical stations. The British experience at Dunkirk and in the Middle East has established certain facts: wounds filled with sulfanilamide are protected from infection for three to five days only; local sulfanilamide does not prevent staphylococcal wound infection; and wounds excised primarily

heal more kindly than those treated with sulfanilamide and delayed surgical care.¹

Current experiments are seeking means of prolonging the effect of topically applied sulfonamides and of potentiating sulfonamide action against the staphylococcus. Hawking² has used various sulfonamide pastes to prevent bacteremia in experimental hemolytic streptococcus infection of wounds in rabbits. Sulfanilamide in an oily base was therapeutically superior to watery suspensions of the drug. However, cod-liver oil caused an especially undesirable tissue reaction, liquid paraffin was moderately bad, and even cottonseed oil, the least harmful, had some ill effect. The most successful results were obtained with a suspension in physiologic saline solution of microcrystals of the relatively insoluble sulfathiazole.

Goldberger³ has reported a potentiated sulfonamide action as a consequence of combination with oxidant antiseptics. Schmelkes and Wyss⁴ and Neter⁵ have demonstrated that chlorine inactivates the inhibitory effect of para-aminobenzoic acid. This same group of investigators⁶ has advanced the hypothesis that the antibacterial effort of sulfonamides is a manifestation of the action of the anionic or zwitterionic species of free dissociated sulfonamide. Inasmuch as all the sulfonamides are weak acids, it has been proposed that a relatively insoluble buffer, such as calcium carbonate, be added to sulfonamide preparations in order to maintain a pH optimal for free dissociation and maximal antibacterial effect. Urea and wetting agents of the triethanolamine type have also been suggested as a means of increasing the solubility and dispersion of topically applied sulfonamides.

Increasing clinical experience with locally applied sulfonamides has recorded instances of excessive absorption of the drug from large wounds and extensive burns. A high blood level of sulfonamide is particularly dangerous when there is depression of renal function from shock or dehydration. Foreign-body reactions and occasional cases of intestinal obstruction have followed the intraperitoneal use of sulfonamides other than the

fairly soluble sulfanilamide. The early reports of the treatment of appendiceal peritonitis with subcutaneously and orally administered sulfanilamide have not been significantly bettered as a consequence of the intraperitoneal use of sulfanilamide. There remains the possibility that the success of local applications depends to some extent on the systemic absorption of the drug.

There is every reason to believe that oral or parenteral sulfonamide therapy offers the most effective control of invasive streptococcal infection. Local sulfonamide therapy introduces a factor of uncontrolled drug absorption, and a deleterious effect on wound healing has been reported. Hence it would seem preferable that civilian injuries receive prompt definitive surgical attention and systemic sulfonamide without local drugs. Local chemotherapy should be reserved for those exigencies of battle wherein no other therapy is possible.

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MEDICAL EPONYM

STILL'S DISEASE

George Frederick Still (b. 1868), medical registrar and pathologist to the Hospital for Sick Children, Great Ormond Street, London, contributed a paper, entitled "On a Form of Chronic Joint Disease in Children," to the Royal Medical and Chirurgical Society of London on April 23, 1896. The communication was read by Dr. Archibald E. Garrod on November 10, 1896, and appears in the society's *Medico-Chirurgical Transactions* (80: 47-59, 1897).

There is a disease, occurring in children, and beginning before the second dentition, which is characterised clinically by elastic fusiform enlargement of joints without bony change, and also by enlargement of glands and spleen.

This disease has hitherto been called rheumatoid arthritis, but it differs from that disease in adults, clinically in the absence of bony change, even when

the disease is advanced, and in the enlargement of glands and spleen, and pathologically in the absence, even in an advanced case, of the cartilage changes which are found quite early in that disease, and also in the absence of osteophytic change.

These differences are not to be attributed merely to modification of disease by difference of age, as there occurs also in children a disease in every respect identical with the rheumatoid arthritis of adults.

R. W. B.

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DEATH

EASTON—ELWOOD T. EASTON, M.D., of Boston, died January 31. He was in his sixty-eighth year.

Born in Rockland, he received his degree from Harvard Medical School in 1899. He became ophthalmic surgeon at the Massachusetts Eye and Ear Infirmary, instructor in ophthalmology at Tufts College Medical School and later professor of that department. He was a member of the Massachusetts Medical Society, the American Medical Association and the New England Ophthalmological Society and held the certificate of the American Board of Ophthalmology.

His widow, three sons, three daughters and three grandchildren survive him.

GATES—ERNEST A. GATES, M.D., of Springfield, died January 4. He was in his seventy-fourth year.

He was a member of the Massachusetts Medical Society, the American Medical Association and the Springfield Medical Club.

His brother and two sisters survive him.

ROBBINS—EUGENE STANLEY ROBBINS, M.D., formerly of New Bedford, died January 18 at West Palm Beach, Florida. He was in his seventy-first year.

Born in Plymouth, Connecticut, Dr. Robbins received his degree from the Bellevue Hospital Medical College, New York, in 1893. He then did postgraduate work in Paris and Berlin. Dr. Robbins was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

WAR ACTIVITIES

CIVILIAN DEFENSE

BLOOD-PLASMA RESERVE

The Medical Division of the United States Office of Civilian Defense pointed out in a recent medical circular that plasma reserves are available in every Civilian Defense region for use in the event of casualties resulting from enemy action or sabotage. The circular emphasizes that this plasma may be used for lifesaving in any disaster. If this plasma is used in nonwar-related incidents, its employment may be considered as a loan, and arrangements may be made later for its replacement, it is pointed out.

Through monthly reports issued by the blood-plasma section of the Medical Division, regional medical officers keep all chiefs of Emergency Medical Service, hospitals and American Red Cross disaster-relief chairmen informed concerning the amount and distribution of plasma reserves

available in their states, and how localities may secure additional supplies in emergencies.

In cities where reserves are stored, they may be obtained by hospitals through the local chiefs of Emergency Medical Service. If a community is without plasma or if its supplies are depleted, the local chief may obtain additional plasma in emergencies from the state chief of Emergency Medical Service.

MISCELLANY

HEMORRHAGE FROM THE TRACHEA, BRONCHI AND LUNGS OF NONTUBERCULOUS ORIGIN

"Hemoptysis," wrote French, "literally means blood spitting, but clinically it is restricted to the expectoration of blood from the lungs, bronchi or trachea." Fifty years ago it was pathognomonic of tuberculosis, with mitral disease as the runner up. These two still dominate the field of etiologic possibilities. It has remained for the bronchoscopist (Jackson, C. L., and Diamond, S. Hemorrhage from the trachea, bronchi and lungs of nontuberculous origin. *Am. Rev. Tuberc.* 46:126-138, 1942) to show us the prominent roles played by other conditions.

The spitting of blood is, of course, the presenting symptom in many and diverse conditions, so the need for painstaking detailed diagnostic study cannot be stressed too strongly. Short cuts and diagnoses by inference are to be condemned.

First, it is necessary to eliminate hematemesis. Useful here is the fact that blood from the lower respiratory tract is usually frothy and bright red, and apt to be mixed with bronchial secretion, whereas that from the stomach ordinarily is dark and often contains particles of food. It should also be noted that in cases of massive hemorrhage, pallor and loss of consciousness are likely to precede a hematemesis whereas in bronchopulmonary bleeding the blood almost invariably is expectorated before signs of actual blood loss appear.

Having by history and careful physical examination eliminated hematemesis and obvious lesions of the larynx and nasal, oral or pharyngeal cavities, one must assume that the source of the blood is subglottic. It is important to note here that the authors believe that, "far too much emphasis has been placed upon varicose veins at the base of the tongue as hemorrhagic foci." (Not a single case was found in their series.)

Once it is determined that the blood is coming from the lower respiratory tract, tuberculosis is the likeliest diagnosis; to quote the authors, "The disease masquerades under many and varied guises." The inquiry must be considered incomplete until the tuberculous or nontuberculous nature of the underlying lesion has been established beyond question.

Tuberculosis having been ruled out, and cardiovascular disease, the blood dyscrasias and acute lobar pneumonia having been eliminated, the search becomes more difficult.

Precise localization and identification of the causative lesion are dependent on supplementary procedures. A comprehensive fluoroscopic and roentgenographic examination of the chest, including planigraphy and bronchography when indicated, is in order in every case of hemoptysis, as well as bronchoscopy, if necessary. As to the advisability of bronchoscopy a patient during or immediately following a hemorrhage, the authors believe that streaking of the sputum is not a contraindication, but

that when frank hemoptysis has occurred, bronchoscopy should not be performed until several days have elapsed since its cessation

What now are the etiologic probabilities? The authors indicate them in the accompanying table, which shows the results of careful diagnostic study of 436 patients re-

Tracheal, Bronchial and Pulmonary Lesions Found in 436 Patients with Hemoptysis

NATURE OF LESION	NO OF PATIENTS IN EACH AGE GROUP AT TIME OF INITIAL HEMOPTYSIS									TOTAL NO OF PA- TIENTS
	LESS THAN 10	10 19	20 29	30 TO 39	40 TO 49	50 TO 59	60 TO AND OVER			
	10	19	29	39	49	59	69	79		
Bronchiectasis	19	25	38	19	20	15	2		138	
Primary carcinoma of bronchus		1	3	9	20	34	15		82	
Tracheobronchitis	4	2	21	12	12	15	8		74	
Pulmonary abscess		4	15	16	9	5	2		51	
No evidence of disease		2	10	14	5	3			34	
Nonpurulent pneumonia	2		3	5	3	1	1		15	
Suppurative pneumonia		1	4	1	2	3			11	
Adenoma of bronchus		3	3	3	2				11	
Secondary cancer of lung				1	1	2	2		6	
Lobar atelectasis		2			1	1			4	
Primary carcinoma of trachea					1	1			2	
Suppurative pneumonia of lymph node discharging into bronchus							1		1	
Non-specific granuloma of bronchus				1					1	
Streptothorax						1			1	
Chondroma of bronchus						1			1	
Osteoma of trachea							1		1	
Dermoid cyst communicating with bronchus				1					1	
Broncholithiasis							1		1	
Neurofibroma involving wall of bronchus			1						1	
Totals	25	41	97	82	76	82	33		436	

ferred for bronchoscopy In the interpretation of this table, it is important to note the following comment of the authors

A great many patients admitted to the hospital with pulmonary bleeding are not seen by the bronchoscopist, the nature of the underlying disease being such that no indication for the direct inspection of the tracheo-bronchial tree is present Included in this category are patients with cardiovascular lesions which lead to the production of chronic passive congestion or pulmonary infarction, patients with acute lobar pneumonia, and patients with blood dyscrasias This group, observed by the internist alone, represents a considerable number of patients with hemoptysis

The authors make the following conclusions

Inflammatory processes are responsible for the hemoptysis in the majority of the cases, the most common etiologic agent being bronchiectasis When one takes into consideration the fact that expectoration of blood is the initial manifestation of carcinoma of the bronchus in only a very small percentage of the patients, it is obvious that bronchoscopy must be done and the diagnosis made early in the course of the disease, before the symptoms have reached the stage of hemorrhage, if a successful therapeutic result is to be achieved in these cases.

Fatal hemorrhage occurred in but 3 of the patients in the series, each of whom had a pulmonary abscess—Reprinted, in part, from *Tuberculous Abstracts* (February, 1943)

ANNUAL PRIZE SUBSCRIPTION

The annual prize subscription offered by the *New England Journal of Medicine* for the best undergraduate contribution to the *Tufts Medical Journal* has been awarded to E Allen Joslyn, '44, for his paper 'Fat Metabolism in Relation to Diabetes,' which appeared in the December, 1942, issue. The paper, 'Cardiac Surgery,' by Mauray Tye, '43, received honorable mention, it appeared in the October, 1942, issue of the journal

BOOK REVIEWS

Surgery of the Ambulatory Patient By L. Kraeger Fergusson, M.D. With a section on fractures by Louis Kaplan, M.D. 8°, cloth, 923 pp., with 645 illustrations Philadelphia J B Lippincott, 1942 \$10.00

The purpose of this book is clearly announced in the challenging statement of the authors, 'It is probable that more poor surgery is performed on minor lesions of the hand than for instance, on major brain lesions' For the surgeon who has mastered the technique of major surgery, much of the general discussion is superfluous But this book will be of greatest help to the general practitioner who only does surgery on minor cases and in whose hands a minor operation may become a major disaster if certain precautions are not followed

Although many of the procedures described may be done on office or hospital outpatients, some are better reserved for hospital inpatients The author states that he has ligated over two hundred saphenous veins as an office procedure. Some surgeons are emphatic in their insistence that this should always be done in the hospital as a full-dress operation However, this is in no way a criticism of the basic material in the book, which is eminently sound The division into symptoms, pathology, diagnosis and treatment makes each section easy to follow, and the illustrations are so well chosen and in such numbers that one can often follow the author by means of them, without reference to the text.

In a work such as this, one hesitates to single out any one portion as superior to the others However, the considerations of breast pathology, low back pain and varicose veins are so good that they seem to deserve special mention

Ambassadors in White The story of American tropical medicine By Charles M Wilson 8°, cloth, 372 pp., with 42 illustrations New York Henry Holt and Company, 1942 \$3.50

The story of American tropical medicine is told by Wilson in an exciting and enthusiastic style Most of the story will be news, not only to the layman but also to the physician who does not know the tropics The names of Gorgas, Walter Reed and Noguchi are familiar to all, but how many of us have more than an inkling of what they did? Still fewer know about the pioneering of Finlay in yellow fever or have heard of the great medical service built up by Deeks for the United Fruit Company

In his first chapter, Wilson emphasizes the transcendent significance of disease in tropical America Although what the author says is true of the peons in certain primitive and unsanitized regions, it is not true of the great cities of Latin America or of the more cultured elements of the population In other chapters the health problems

arising from a few of the more important diseases of the tropics are presented briefly. There are also vivid sketches of outstanding personalities upon whom praise has been generously bestowed. A few inaccuracies of no great importance were noted by the reviewer, and some of the information about disease is out of date.

The reviewer regrets being obliged to point out that on pages 200, 201 and 202, in his sketch of Noguchi's work, Wilson has criticized unfairly the research of a Harvard expedition to Peru. Not only has the author been ill-informed, but the tone of some of his remarks is offensive. Noguchi would never have assumed this attitude. Noguchi, moreover, would have recognized the fact that, at a time when his *Leptospira icteroides* had received general acceptance as the cause of yellow fever, skepticism persisted at Harvard. This skepticism culminated in a series of well-planned experiments by Sellards and Theiler which proved beyond a shadow of doubt in 1926 and 1927 that *Leptospira icteroides* and *L. icterohaemorrhagiae* were identical, and that a leptospira was not the cause of yellow fever.

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Acute Injuries of the Head: Their diagnosis, treatment, complications and sequels. By G. F. Rowbotham, B.Sc. (Manch.), F.R.C.S. (Eng.). With a foreword by Norman M. Dott, M.B., Ch.B. (Ed.), F.R.C.S. (Ed.). 8°, cloth, 288 pp., with 124 illustrations. Baltimore: The Williams and Wilkins Company, 1942. \$7.50.

"This book is written primarily for those who are responsible for the treatment of acute cerebral trauma and who have not received special training in neurosurgery or neurology." Every hospital must care for patients with acute craniocerebral injuries, and usually the small institutions do not afford good treatment because of a disinterested profession. It is essential that general surgeons who are called on to treat such patients know the main points of diagnosis on which treatment is based. They should recognize the indications for exploration of the cranial vault, for subtemporal decompression and for the treatment of compound fractures of the skull. This book furnishes a concise review, which may serve as a guide to the correct handling of craniocerebral injuries.

There are some well-chosen illustrations on operative technic. The last chapter, "Sequels of Head Injuries," is the best of the whole book. This aspect is one of the most important but often most neglected of the entire subject. The description of the post-traumatic syndrome could not be better done than it is in the author's depiction of such a patient in the physician's office.

A few items in the book deserve mention because of their variance with American practice. The author does not encourage, but he does allow, the use of morphine after head injuries in ¼-gr. doses; whereas in this country the drug is considered to be absolutely contraindicated in

such cases. In the author's experience of 25 cases of middle meningeal hemorrhage, all had a lucid interval; the many exceptions to this are not stressed sufficiently. It is stated that patients with craniocerebral injuries can usually be up and about in three weeks, with gradual mobilization during this period. In the reviewer's experience, probably no single factor can prevent development of the postconcussion syndrome more than absolute rest in bed; in severe injuries this should be continued for at least three weeks, and as long after that as symptoms are present.

Handbook of Health for Overseas Service. By George C. Shattuck, M.D., with contributions by other authors. 24°, cloth, 198 pp., with 14 illustrations. Cambridge, Massachusetts: Harvard University Press, 1942. Not for sale (copies may be obtained gratis from the Harvard University Press).

This volume was prepared for the Co-ordinator of Information, Washington, D. C., now known as the Office of Strategic Services. Its purpose is to act as a guide for nonmedical men who travel in places where medical services are not available. It covers such subjects as food, drinking water, camp hygiene, clothing and first aid, with a brief discussion of many diseased conditions that may be encountered. Although all diseases are not included, it is reasonably comprehensive, covering ailments of the tropical and arctic regions. A list of the drugs and surgical equipment that should be available are included, although these necessarily are limited in number.

The volume is compact, has a flexible cover and can easily be carried in the pocket. It should be of great value to men going on field service and can safely be recommended by the physician to patients so situated that immediate medical attention is not available.

Doctor Bard of Hyde Park: The famous physician of Revolutionary times, the man who saved Washington's life. By John B. Langstaff. Introduction by Nicholas M. Butler. 8°, cloth, 365 pp., with 11 illustrations and frontispiece. New York: E. P. Dutton and Company, Incorporated, 1942. \$3.75.

This is a carefully written and well-documented life of one of the outstanding Revolutionary physicians who practiced in New York City during the latter part of the eighteenth century. He was a physician at one time to George Washington and served as president of the College of Physicians and Surgeons. He later retired to Hyde Park on the Hudson, and the title of the book is taken from this relatively unimportant period of his life. The interest in Bard is largely through the development of the New York Hospital, his operation on George Washington for a severe carbuncle and the pleasant stamp that he gave to medicine during his time. He was an excellent example of the English gentleman physician, in direct line with Lettsom and Fothergill. The author has done an excellent piece of work in collecting the data. He has long been associated with the medical profession for he has served as chaplain of the Bellevue Hospital and is the son of a well-known physician. He descends, moreover, from physicians who were active in New York in Bard's time. This is an important biography and should be widely read.

(Notices on page xiii)

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VASCULAR AND NEUROLOGIC LESIONS IN SURVIVORS OF SHIPWRECK

II. Painful Swollen Feet Secondary to Prolonged Dehydration and Malnutrition

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THE true immersion-foot syndrome described in the first part of this paper¹ is caused by direct thermal injury to the tissues short of actual freezing. It develops after relatively brief periods of contact with water at temperatures below 50 or possibly even 60°F. A superficially similar, but fundamentally quite different, condition has developed after exposure to warm water and bright sunshine in survivors of torpedoed vessels who have been adrift in the Gulf Stream without an adequate supply of water and food for periods of over two weeks. These individuals may show no evidence of direct cutaneous injury, but yet complain of an equal degree of edema and sensory disturbance. This condition has also been called "immersion foot," but the term is inappropriate in this connection and should be given up.

The cases on which this report is based were seen in a United States Marine Hospital, through the courtesy of Captain W. S. Bean, the commanding officer, a member of the United States Public Health Service. He and his staff have permitted me to add the results of their clinical findings to my own, as well as to make use of their laboratory determinations. The deductions drawn from these data are my own and do not necessarily represent the views of the United States Public Health Service. These survivors of two lifeboat crews have already been the subject of a more detailed report for the Medical Corps of the United States Navy,² which will be briefly summarized here in order to point out that there are two fundamentally different conditions that may lead to much pain and incapacity following the sinking of ships at sea in the present war. Since the more complete report was written, new clinical and laboratory data have been furnished me by Drs. Richard H. Smith and Leo Waitzkin of the United States

Public Health Service. This has necessitated a number of minor changes in the evidence presented and in the conclusions to be drawn therefrom.

It should be emphasized at the outset that the syndrome reported here is different in many respects from that observed after immersion in cold water.¹ With these southern survivors, both vessels were torpedoed in relatively warm water (around 70°F) in southern latitudes during the month of April. The men were adrift for sixteen and seventeen days respectively. Owing to the fact that their ships were torpedoed well off the usual trans-Atlantic shipping lanes and they could not hope for early rescue, their allowance of water was progressively reduced from 16 ounces to a bare 5 ounces a day. With the intense sunshine and heat by day, coupled with the hard work of bailing and handling the boats, both crews developed such severe dehydration that they were unable to swallow the concentrated solid ration of pemmican, hardtack and chocolate. After the first few days all that the men were able to swallow was a small amount of malted-milk powder dissolved in their half-cup of water. Three out of six West African Negroes in the crew of lifeboat A drank salt water and died. All the crew members of lifeboat B survived. The men in both boats were so crowded that they were forced to sit close together with their legs dependent and to sleep in this position. After a week adrift under these circumstances nearly all the men noticed that their feet were becoming greatly swollen and numb; in addition they began to have a peculiar tingling and aching sensation in the soles. Some noticed similar symptoms in their hands but of lesser degree. The swelling and sensory disturbances in the legs were distinctly less noticeable in the men who had been able to move about the most. A few who took turns as steersman were able to

¹Released for publication by the Division of Publications of the Bureau of Medicine and Surgery, United States Navy.

stretch their legs out horizontally during their watches; others realized that the circulation in their feet was improved and the swelling was lessened by flexing and extending their feet and toes. A number of the men in lifeboat B who went over the side on several occasions to swim alongside commented on the improvement in the condition of their lower extremities. On finally being rescued, all were deeply tanned, and many had developed cracks and small crusted lesions due to exposure to wind and salt water. When they came aboard the rescuing vessels most of the men found that walking on their swollen feet was difficult, and that without support they lost their balance because of numbness in their feet and loss of sense of position. In addition the majority complained of deep plantar tenderness and pain. These exact complaints are also common in sailors rescued after immersion in cold water.¹ On their arrival at the hospital, all the men were suffering from exhaustion, malnutrition and dehydration.

The crew of lifeboat A had wet feet throughout the entire voyage, as their boat leaked continuously. During the last two days, when they sailed out of the warm water of the Gulf Stream and approached the coast, the temperature of the sea water fell to around 50°F. (below the critical level at which thermal injury can occur). As a result of this exposure several of the men, notably the West African Negroes (Cases 6, 7 and 8), ran a low-grade fever (99 to 101°F.) for several weeks* after rescue and developed changes in their feet characteristic of exposure to cold. These consisted of patches of superficial gangrene, blebs and sluggish circulation in the cutaneous capillary bed, with a subsequent hyperemic phase after rescue. This condition, however, was pronounced only in the Negroes and was much milder than that generally seen after exposure in northern waters.¹ The crew of lifeboat B were exposed to cool air and suffered from cloudy, heavy weather the first five days, so that their clothes were continuously wet. The weather then cleared and by day "the heat became almost unbearable. . . . Relief was obtained by going overside and swimming. Feet were also soaked in buckets of water. . . . Feet were kept dry except when soaked in buckets during heat of day." The crew of this lifeboat were therefore never exposed to water below 70°F. and showed no signs of cutaneous injury from cold.

After examining these men it was at once apparent that their condition differed fundamentally from that of the survivors seen after rescue from the colder waters of the North Atlantic. Although both groups suffered from swollen and painful feet, many of these survivors of shipwreck in rela-

tively warm water did not bear evidence of tissue damage in their feet, and they had other systemic disturbances of a very different nature. These consisted of slight but definite swelling and subjective sensory disturbances in the hands, as well as the more obvious changes in the feet; many of the men were also found to have glossitis and stomatitis, and additional gastrointestinal complaints. The clinical findings observed in the entire series are summarized in Table 1, and the laboratory determinations in Table 2.

As pointed out above, some direct tissue injury from cold undoubtedly occurred in the crew of lifeboat A during the last two days of their voyage, when they left the warm waters of the Gulf Stream. This was definitely not the case in the men of lifeboat B. But with them, and to a large extent with the men of lifeboat A as well, it is evident that other reasons must have accounted for the greater part of the swelling, which often extended to the knees,† as well as the tenderness and other sensory changes, which involved the feet and, in some cases, the hands as well. Other contributory factors which might account for these findings are the following:

(1) *Continued dependency of the legs.* Hypostatic edema is always a factor after a voyage in a crowded lifeboat of prolonged duration when there is no space to stretch the legs out horizontally and men are forced to sleep in a sitting position.

(2) *Hypoproteinemia.* As a result of extreme dehydration, these men had been unable to swallow any solid food after the first few days adrift. In addition, they were forced to row and bail, the energy for which had to be provided from their own tissues. As a result it is not surprising that many were found to have a serum protein below the critical level at which edema develops. The low albumin-globulin ratio in Cases 1 and 7 is of particular significance. From the experimental work of Jones, Eaton and White⁸ on nutritional edema in animals, it is probable that the swelling in the legs of these men was far less marked during the period that they were adrift and critically dehydrated, and that it developed rapidly as they were able to restore their depleted tissue fluids. There was also a progressive fall in serum protein in the course of rehydration, which is well exemplified by the serial determinations made in Case 1.

(3) *Vitamin deficiency.* One is led to speculate whether the intense aching pain and deep plantar tenderness complained of by these survivors during the last week at sea and in the

*In the case of uncomplicated thermal injury to the feet from cold, the febrile reaction usually subsides within thirty-six hours.²

†The changes due to cold water generally involve only the feet and lower third of the legs.²

TABLE 1. Clinical Data on Southern Survivors.*

CASE No.	SEX	EXTENT OF LESION	CUTANEOUS CHANGES	REFLEXES	SENSORY CHANGES	MUSCLE TENDON-ITIS	PAIN	STATUS TITUS	DAY OF DISCHARGE	COMMENT
CREW OF LIFEBOAT A										
1	79	++	Superficial gangrene in toes 5 (4), amputation in toes 1, 3, 4 and 5 (1).	+	Hypaesthesia and tingling in distal half of feet	+	0	++	20th	Patient had severe degree of malnutrition and diarrhea for a month preceding trip. In lifeboat he covered on floor boards without moving. His general condition was precarious at first, he was semicomatose and had diarrhea with occult blood. Thermal injury to the feet was definite.
2	26	+	0	+	0	0	0	0	20th	Patient exercised feet during period of dependency.
3	22	±	Several small areas of necrosis and dequamation	++	Skin of feet and lower legs hypersensitive	0	0	+	31st	Patient exercised feet while in lifeboat, and evidence of thermal injury was not marked. Neuritis appeared within a week, but he developed a severe stomatitis 3 days after rescue, with fever and leukocytosis. This was cured within a week after treatment with vitamin B.
4	32	0 (formerly present)	0	+	Numbness at first when walking, hypaesthesia wore off distally, disappearing in 3 weeks	0	++	0	20th	Patient exercised feet while in lifeboat. Neuritis gone in a week.
5	35	+	0	-	Hypaesthesia receded to toes in 3 weeks	0	0	0	20th	
6	23 Negro	++	Deep cracks and blisters in skin of soles, with eventual sloughing	+	Impossible to evaluate owing to large edema of feet	+	+++	0		Patient exercised feet 3 days. On 1st day severe inflammatory reaction, which receded in 3 days. On 3rd day cold water was used to treat feet for 9 days. Feet were healed after 2 weeks without vitamin therapy.
7	57 Negro	++	Dequamation and epidermophytosis, hands also swollen at first	+	Pain and sensory changes in hands for 2 weeks, receding to distal half of feet present after 3 weeks	-	+	0		Patient's bare feet were in water most of the time. Pain started after 3 weeks. On 5th day severe hyperemia of feet, which receded in 3 weeks. Patient exercised feet 3 days, but it was not cured. Thermal injury was severe, and probably cured.
8	39 Negro	+	0	+	Hypaesthesia at first in ankles, receding to toes in 3 weeks	0	+			Thermal injury to feet, with severe inflammation of feet. Temperature of feet normal. Patient exercised feet 3 days. No vitamin therapy given. Thermal injury was less marked than in cases 6 and 7.
CREW OF LIFEBOAT B										
9	33	0	0		0	0	±	+	14th	Patient exercised at 1st in general condition.
10	44	0	0		Hypaesthesia of feet, subjective changes in hands	+	++	0	14th	Patient exercised but made good recovery.
11	50	R++ L+	0		Hypaesthesia and paresthesia, subjective changes in hands	+	+	+	14th	Neuritis disappeared in 3 days.
12	35	0	Superficial crusted areas due to sun and windburn		Sensation objectively normal but subjectively abnormal in hands as well as feet	+	+	+	14th	Sensory disturbances disappeared before discharge.
13	24	±	0		Sensation objectively normal but subjectively abnormal in hands as well as feet	+	+	+	14th	
14	32	0	0		Distal half of feet hyperaesthetic, hands to lesser degree	+	+	0	14th	Neuritis disappeared in 3 days.
15	25	0	0		Subjectively both hands and feet feel abnormal	+	++	0	14th	Neuritis cleared quickly.

*Crew of lifeboat A examined 3 weeks after rescue, those of lifeboat B, 2 days after rescue.

hospital could be caused solely by edema secondary to dependency and hypoproteinemia. It appears most unlikely that this could have been the case, and it is not possible to explain hypesthesia and ataxia of the feet, and similar sub-

showed normal responses in the 4 patients tested. This is incompatible with the advanced type of neuritis due to long-standing avitaminosis, but in no way rules out the earlier stages, which might occur in such a relatively brief period.

TABLE 2. Available Laboratory Data on Southern Survivors.*

CASE No	DATE	SPECIFIC GRAVITY OF URINE	RED CELL COUNT × 10 ⁶	HEMOGLOBIN gm	WHITE CELL COUNT × 10 ³	TOTAL PROTEIN gm./100 cc.	BLOOD			UREA NITROGEN mg./100 cc.	CHLO-PIDE mg./100 cc.	ASCOR-BIC ACID mg./100 cc.	PROTHROMBIN TIME sec.	CLINICAL RECORD IN FEET
							ALBU-MIN	CLOTE-LIN						
1	4/15/42	1.025	—	—	—	—	—	—	—	—	—	—	—	—
	4/16/42	—	4.00	15.3	12.3	5.4	3.5	4.0	24.0	—	—	—	—	+
	4/20/42	1.019	3.61	13.3	10.9	3.3	1.7	1.6	—	—	—	—	—	—
	4/27/42	1.018	—	—	—	4.8	2.8	2.0	—	—	—	—	—	—
	5/7/42	—	—	—	—	5.4	3.3	2.1	—	—	—	—	—	—
2	4/15/42	1.030	—	—	—	—	—	—	—	—	—	—	—	—
	4/17/42	—	5.58	13.7	8.7	—	—	—	—	—	—	—	—	—
3	4/15/42	1.018	—	—	—	—	—	—	—	—	—	—	—	—
	4/17/42	—	5.89	13.3	15.1	—	—	—	—	—	—	—	—	—
4	4/15/42	1.025	—	—	—	—	—	—	—	—	—	—	—	—
	4/17/42	—	4.63	16.4	5.4	—	—	—	—	—	—	—	—	—
5	4/15/42	1.025	—	—	—	—	—	—	—	—	—	—	—	—
	4/17/42	—	5.09	14.0	9.6	—	—	—	—	—	—	—	—	—
6	4/17/42	—	3.63	10.5	13.9	—	—	—	—	—	—	—	—	—
	4/24/42	—	4.35	11.0	8.3	—	—	—	—	—	—	—	—	—
7	4/15/42	1.025	—	—	—	—	—	—	—	—	—	—	—	—
	4/17/42	—	4.99	13.3	10.0	—	—	—	—	—	—	—	—	—
	4/18/42	—	—	—	—	5.1	2.4	2.7	13.3	770	—	—	—	—
8	4/15/42	1.020	—	—	—	—	—	—	—	—	—	—	—	—
	4/17/42	—	4.06	12.9	6.9	—	—	—	—	—	—	—	—	—
9	5/8/42	—	—	—	—	6.0	—	—	—	—	410	1.98	27	0
10	5/8/42	1.012	4.68	12.4	15.6	—	—	—	—	—	390	1.82	25	—
	5/9/42	—	—	—	—	5.6	—	—	—	—	—	—	—	+
	5/13/42	—	5.05	12.1	6.9	—	—	—	—	—	—	—	—	†
11	5/8/42	1.023	—	—	—	—	—	—	—	—	—	—	—	—
	5/9/42	—	—	—	—	—	—	—	—	—	—	—	—	+
	5/14/42	—	—	—	—	—	—	—	—	—	—	—	—	0
12	5/8/42	1.014	—	—	—	—	—	—	—	—	—	—	—	+
13	5/8/42	1.023	—	—	—	—	—	—	—	—	—	—	—	0
14	5/8/42	1.025	—	—	—	—	—	—	—	—	—	—	—	+
15	5/8/42	1.029	—	—	—	—	—	—	—	—	—	—	—	—
16†	—	—	—	—	—	—	—	—	—	—	—	—	46	—

*The figures do not show the striking alterations in the blood and urine which go with severe dehydration, but it must be remembered that these men had already had up to twenty-four hours to restore their depleted body water reserves before any of the above determinations could be made. Other compensatory factors must also be taken into account. Although Cases 2 and 3 show a definite erythrocyte concentration, the anemia that goes with starvation would counterbalance this. All the serum protein levels are low, and would probably have gone lower, as was so in Case 1, if further estimations had been made after the water balance had returned to normal levels. Half the patients still had a urinary specific gravity of 1.025 or higher after nearly a day's unlimited access to water. The blood urea nitrogen level of 24 mg. in Case 1 is distinctly elevated and the figure of 13.3 mg. in Case 7 is not significant, as it was not obtained until three days after rescue. Loss of blood electrolytes was pronounced in Cases 9 and 10. This was presumably caused by excessive sweating with a low salt intake, whereas the patient in Case 7, who had drunk salt water, had a very high level. The ascorbic acid figures in Cases 9 and 10 are not reduced.

†This patient, not included in the study because he had just been operated on for gastric hemorrhage, had the highest prothrombin time observed.

jective disturbances of the hands, on this basis. This picture is more suggestive of a deficiency in the antineuritic factor in the vitamin B complex, such as is seen in alcoholic neuritis. Examination of the knee jerks in these subjects

Further clinical findings that suggest an avitaminosis were the oral lesions. Of the patients examined, Cases 1, 3, 9, 11, 12 and 13 reached the hospital with a nonspecific stomatitis. This consisted of superficial vesicles and ulcers of the

tongue, buccal mucosa, palate and pharynx. In Cases 1, 9 and 12 the sides of the tongue were smooth and reddened, and the patient in Case 13 had suffered from bleeding gums. It is also of interest to note that in 7 out of 9 patients where the feces were examined with the guaiac and benzidine reagents, the tests were at first positive for occult blood (Cases 1, 10, 11, 12, 14, 15 and 16). It is of further interest that in the 3 patients in whom the prothrombin times were determined, there was an increase beyond the normal period of 20 seconds to 40, 27 and 25 seconds, although there is some question concerning the accuracy of these figures. If the values are correct, they denote a definite deficiency in vitamin K, which reached a severe degree in Case 16. This man, who had a history of chronic indigestion, became severely exsanguinated from a bleeding gastric ulcer, which finally necessitated surgical intervention. Another survivor in the same hospital, who had been rescued after a long period adrift in warm water, also suffered exsanguinating gastric hemorrhages, from which he died. It is possible that this bleeding from the gastrointestinal tract, as well as the stomatitis, is related to nicotinic acid deficiency, since ulcerations may occur at any level in the gastrointestinal tract in the deficiency state. Further studies on the role of vitamin deficiency in shipwreck survivors are urgently needed before any definite conclusions can be drawn.

Heretofore, the signs of alcoholic neuritis and pellagra have not been known to occur in as brief a period as a fortnight. In fasting subjects who have been studied for longer periods, sensory changes in the extremities have not been recorded, but these observations have been made on inactive persons. The fact that thiamin, nicotinic acid and riboflavin play an active chemical role in the oxidation of glucose may explain their rapid depletion in these survivors. A depletion of the antineuritic and other components of the vitamin B complex is, therefore, a distinct possibility. It is also possible that the men who suffered the most were in a partially depleted state before their ships were torpedoed and their vitamin intake stopped. This was certainly true in Case 1, but I was unable to discover any evidence of this in the other men.

In order to obtain further information concerning the possibility that vitamin deficiencies arise in such a short period of time, I consulted two authorities on vitamin deficiency, Dr. John B. Youmans, associate professor of medicine at Vanderbilt University School of Medicine, and Dr. W. H. Sebrell, chief of the Division of Chemotherapy of the United States Public Health Service. Dr. Youmans wrote:

Patients with nutritional edema very frequently develop pain and tenderness, and sometimes superficial inflammation (erythema), particularly when the onset is rather abrupt. . . . With a very restricted diet and with hard work, some deficiencies such as that due to vitamin B₁ are believed to develop evidence of the deficiency within a week or so. . . . The stomatitis and glossitis may well represent a combination of a deficiency of the vitamin B complex, including riboflavin plus dehydration. Dehydration is quite important as there is evidence that this precipitates the syndrome of pellagra.

Dr. Sebrell, who subsequently saw some of this group of patients, states that his "impression is that thiamin and nicotinic acid deficiencies are definite possibilities." When further similar cases can be located he is prepared to make special tests to give accurate information about the thiamin and nicotinic acid levels. Examination of the scleras by the slit-lamp for peripheral vascularization and of the lips and mouth by experts in riboflavin and nicotinic acid deficiency will answer this question with certainty.

Unlike the more severe thermal injuries suffered by the survivors of vessels torpedoed in the North Atlantic, where vascular thrombosis and sepsis may necessitate amputation, the peripheral lesions of the cases from southern waters were not serious and required over a fortnight's hospitalization in only 6 cases. Three of these were the West African Negroes who undoubtedly had complicating injuries from immersion in cold water and less evidence of a vitamin deficiency than their Anglo-Saxon crew mates. The possible increased sensitivity of the West African Negroes to cold and their greater resistance to dietary deficiency will be a point of interest for further investigation. In examining the northern survivors I had been impressed by the fact that the reaction caused by immersion in cold water rarely extended much above the ankles, whereas in these cases it rose nearly to the knees. The edema subsided promptly on bed rest, elevation of the legs and an adequate diet. The most incapacitating symptom was the neuritic pain in the feet. These persisted for nearly two months in the 3 Negroes, 2 of whom were not given special vitamin therapy. Whether due to specific action or merely coincidentally, the neuritic manifestations disappeared within a period of three to ten days in the other men after a high intake of vitamin B.

In evaluating these survivors of exposure, malnutrition and dehydration, it seems reasonable to conclude that the men of lifeboat A suffered injury from cold of slight but definite degree. This, however, falls far short of explaining the entire clinical picture that they presented. Although the crew members of lifeboat B were generally

chilled by the cloudy, heavy weather of the first five days, thereafter they suffered from intense heat and their feet remained dry except when they wet them for relief. Their most striking symptoms—edema to the knees, sensory disturbances, which in some cases involved the hands as well as the feet, stomatitis and ulceration of the gastrointestinal tract—must be accounted for on a basis other than immersion in cold water. These conditions made their appearance slowly, the first tingling and pain developing at the end of a week. The edema can be readily explained by the prolonged dependency and protein deficiency. Whether the sensory disturbances and ulceration of the mucous membranes of the digestive tract are wholly or merely in part due to vitamin deficiency must require final proof from future more complete studies. Opportunities for such studies are now frequently present, particularly in the war in the South Pacific.

In the matter of treatment, much can be accomplished prophylactically by furnishing a more suitable lifeboat ration for vessels on tropical voyages. One of the hard facts brought out by the present naval war is that dry, concentrated foods are worse than none at all when water is scarce. Although the problem of supplying a more satisfactory ration remains to be worked out, an adequate intake of the various components of the vitamin B complex can be supplied very simply and inexpensively by tablets of brewer's yeast.* The protective properties of fresh meat are well known, and whenever this can be obtained in the form of birds, fish or shellfish, the raw meat, blood, liver and other viscera can, with few exceptions,⁴ be consumed with safety. It is of interest in this connection that Captain Bligh's company, in the famous voyage from Tofoa to Timor after they were cast adrift by the mutineers on the *Bounty*, did not develop any symptoms of neuritis after six weeks on starvation rations supplemented by small quantities of fish, mussels and eggs of sea birds.⁵ Judging from the experience of Dixon, Pastula and Aldrich,⁶ who navigated the South Pacific for thirty-four days in a small rubber raft, an adequate diet can be obtained in many parts of the tropical seas if the lifeboat or raft is equipped with a small-caliber shotgun of rustless steel and a hand line or two. Richards and Bani-gan,⁴ the authors of a very practical manual on how to abandon ship, point out that a fish spear is more useful than a hook and line—"Your hook either will be taken by a large fish, which will

snap your line, or a small fish, which will be devoured before you can draw it in."

The skin can be protected against salt-water blisters in the tropics and also against cold by greasing¹; therefore a liberal supply of heavy oil should be included in all lifeboat stores. In intense sunshine the skin must also be protected by some form of clothing and, if possible, by rigging an awning over the boat. Any constricting clothing about the legs or tight shoes should be removed. In addition to greasing the feet, stretching the legs out horizontally and forcibly flexing and extending the toes are of great value in reducing edema and stiffness of the muscles. Weather and absence of sharks and barracuda permitting, getting into the water and paddling alongside the boat has been found extremely helpful by all the sailors who have tried it. This not only prevents loss of water by sweating, but the muscular movements in a horizontal position increase the flow of lymph and return a considerable quantity of edema fluid to the circulation.⁷

When survivors are picked up they should be lifted on board the rescuing vessel and carried below to prevent further damage to the skin of their insensitive, swollen feet. If there is injury to the skin from sun and salt-water burns, prevention of sepsis is important. This and the care of cold-water injuries have been described in the first part of this paper.¹ Further local treatment should include elevation of the swollen legs, Buerger's postural exercises and physiotherapy, if carried out in a hospital by an experienced person.

The most urgent need of these survivors at the time of rescue is the proper treatment of their dehydration and malnutrition. This treatment is carried out along standard lines and will not be discussed here. In addition to a high protein intake, such patients should be given a therapeutic test of vitamin B in large amounts, with daily intramuscular injections of thiamin chloride, 50 mg., and Lederle's vitamin B complex, 10 cc. (this contains thiamin, nicotinic acid and riboflavin). If the response is favorable, it will go far to establish the diagnosis of vitamin B deficiency. Once this point has been settled, a less expensive therapy consisting of brewer's yeast (which contains large amounts of all the vitamin B components) and a diet of green vegetables, carrots, butter and liver can be substituted.

SUMMARY AND CONCLUSIONS

The painful swelling of the feet observed in two lifeboat crews, adrift for prolonged periods in the Gulf Stream, had fundamental clinical and etiologic differences from the "immersion-foot" syn-

*More concentrated preparations are available that contain reasonable proportions of the various components in the vitamin B complex. Among these are Unicaps (Upjohn) and Vitamin B Complex Capsules (Lederle).

intercellular and extracellular edema in the epidermis.¹¹ The blood vessels in the corium are increased in number and are dilated, but little cellular infiltration is present and there is no endovasculitis or perivascular infiltration. Slight edema is present, as well as dissociation of the connective-tissue fibers of the corium.

Through the work of many investigators, it has now been shown that this disease in rats is due to the existence in the egg white of a substance that binds the biotin in the diet, preventing its absorption.² The specific constituent responsible for this effect has now been concentrated and purified.^{12, 13} It is a proteinlike substance called "avidin" (an abbreviation for avidalbumin, meaning "hungry albumin"). This concentrated preparation can replace raw egg white as the toxic factor necessary for the production of egg-white disease, but it must be given orally, since with parenteral administration it actually has a curative action.¹⁴ The latter phenomenon is presumably due to the fact that concentrates of avidin consistently contain some biotin, which is liberated in vivo. The only source of avidin thus far known is egg white.

The avidin-biotin compound under the conditions of the intestinal medium is a stable one and is excreted in the feces as such,¹⁵ but may be broken up by steaming or by acid hydrolysis. Avidin loses its toxic effect if the egg white is heated at 100°C. for three to thirty minutes.^{2, 16}

Animals with egg-white disease recover rapidly when placed on a normal diet and when the ingestion of egg white is stopped. They also recover even when continued on the same diet provided that adequate quantities of vitamin H (biotin) are administered. The latter is from three to five times more effective when given parenterally than when given orally.¹⁷

The identification of vitamin H¹⁸⁻²⁰ (the curative factor of egg-white disease in rats) as biotin²¹ (a growth factor for yeast) and as coenzyme R²² (a growth and respiration factor for many strains of legume-nodule bacteria) has eliminated the necessity of animal assay for the estimation of biotin and has allowed substitution for it of a simpler and quicker microbiologic method. When yeast is used as the test organism,²³ the bioassay can be performed in less than twenty-four hours.

Although biotin is widely distributed in the various articles of diet, it is found in the greatest concentrations in liver, kidney, yeast, cow's milk and pancreas.²⁴⁻²⁶ It is present in egg yolk in a high-molecular, undialyzable form, which is physiologically active in yeast-growth tests or in tests made on rats with egg-white disease.²⁷ A whole egg, however, contains a distinctly greater amount

of avidin than can be neutralized by the biotin of the whole yolk.²⁷

Biotin is insoluble in water in its natural state as it occurs in liver, kidney or yeast.²⁴ For the complete extraction of biotin, commonly present in bound form in foodstuffs and similar products, acid hydrolysis is, in general, the most suitable procedure.^{23, 26, 28-30}

Biotin was first obtained in crystalline form in 1936 in Kögl's laboratory from egg yolk.²¹ The empirical formula was reported in 1938.³ Du Vigneaud and his collaborators^{20, 31} have isolated biotin from the liver as the pure crystalline methyl ester, the physical and chemical properties of which are in close agreement with the empirical formula $C_{11}H_{18}O_3N_2S$. Their later studies^{32, 33} led to the recognition of certain functional groups of biotin, permitting them to conclude that it is a carboxylic acid containing an N, N'-substituted cyclic urea grouping and possessing sulfur in a thio-ether linkage.

CASE REPORT

R. M. (No. 1042432), a 66-year-old retired Italian laborer, was admitted to the Boston City Hospital on October 8, 1941, complaining of a chill, fever and cough. The routine clinical analyses revealed that he had a urinary-tract infection, chronic bronchitis, emphysema, arteriosclerotic heart disease (with mild congestive failure), amputated penis and exfoliative dermatitis—the last being of particular interest so far as this paper is concerned. There was no history of medication or of exposure to chemical agents to account for the rash. His dietary history was, however, significant.

Since adolescence the patient had been extremely fond of raw eggs, putting one or two into each glass of wine that he took. For several decades he had drunk wine or whiskey almost every day. During the six years preceding admission he had drunk from 1 to 4 quarts of wine daily. In order to have a sufficient number of eggs for his drinks, he deserted his family and moved to the country so that he could maintain his own chicken farm. During this period of time he ate from two to six dozen raw eggs per week. He did not eat at any regular time. Sometimes he ate only one or two meals a day, and sometimes he drank nothing but wine and eggs for 1 or 2 days. His choice of foods was narrow and consisted chiefly of canned goods; rarely did he drink milk or eat liver (sources of biotin).

So long as he could remember, his skin had been quite red, but 5 years previously the redness increased and many scales were noted. A mild conjunctivitis had been present for several months. These changes persisted, and 3 months before admission there was an increase in their severity. There was not much fluctuation in the nature of the rash. There was never any itching, vesicles, bullas or evidence of skin infection; nor was there diarrhea, sore tongue, neuralgia, cheilosis, night blindness or hemorrhagic phenomena.

In March, 1941, the patient had a partial amputation of the penis because of a carcinoma. Owing to a recurrence of the neoplasm, a more radical amputation was

performed in September, 1941. On October 8, he had a chill and fever and was readmitted to the hospital.

On examining the skin, about half the total surface (chiefly the trunk) appeared normal, but the entire face, ears, shoulders, dorsum of forearms, hands and lower legs were fiery red and covered with many medium sized

keratinization; masses of keratinized material are separated from the underlying epidermis and there is slight parakeratinization. Intracellular and extracellular edema in the stratum mucosum is present.

The corium is thickened, owing to interstitial edema and hypertrophy of the collagen fibers. The fibers



FIGURE 1 Section of Skin.

Note the loose sheet of keratinized epithelium, the absence of rete pegs and the cellular infiltration around the hair follicles, sweat glands and blood vessels.

scales. The involved areas were sharply demarcated from the normal skin. On the trunk the lesions were small and scantily scattered. There was no elevation of the skin, no raw surfaces and little if any edema. There was slight palpebral edema and moderate conjunctival injection, but no corneal vascularization. The tongue was grayish red, but there was no papillary atrophy.

The urine showed a + test for albumin, and the sediment contained many white cells, occasional red cells and no casts. Cultures of the urine repeatedly grew colon bacilli, enterococci, *Staphylococcus aureus* and occasionally *Proteus vulgaris*. The hemoglobin was 78 per cent. The white-cell count was 17,000, with 91 per cent polymorphonuclear leukocytes, 5 per cent lymphocytes and 4 per cent monocytes. A blood Hinton test was negative.

A biopsy of the skin was taken on October 10. The sections were studied by Drs. Frederic Parker, Jr., Howard T. Karsner, William R. Hill and several other pathologists. A specific diagnosis was not made, but a summary of the observations is as follows:

There is a sharp distinction between the corium and epidermis (Fig. 1). The rete pegs are flattened and in some areas they do not extend downward into the corium, leaving a flat line between the two layers. Some of the hair follicles and sweat ducts are plugged. The epidermis is of normal width but there is hyper-

keratinization; masses of keratinized material are separated from the underlying epidermis and there is slight parakeratinization. Intracellular and extracellular edema in the stratum mucosum is present. The corium is thickened, owing to interstitial edema and hypertrophy of the collagen fibers. The fibers adjacent to the epidermis are homogeneous and pale; the middle and deep fibers are thickened, but otherwise normal. The sebaceous glands are absent, the hair follicles atrophic, the arrectores pilorum muscles hypertrophic, and the sweat glands and ducts dilated. A few acini of the sweat glands are necrotic. The elastic-tissue fibers are absent in the papillary bodies and decreased throughout the cutis, except in a band in the region of the superficial capillaries, where they are increased in number and the individual fibers hypertrophic. In the deep cutis they are hypertrophic but few in number. The subcutaneous fat and nerves are normal. In the upper corium are numerous areas of cellular infiltration, involving particularly the sweat glands and the blood vessels (Fig. 2). The cells are chiefly polymorphonuclear leukocytes and lymphocytes, with a few plasma cells. The vasculitis involves chiefly the superficial vessels, since the deeper vessels of the corium are normal. The vessels in the upper cutis are increased in number and show endothelial proliferation.

The significance of these histologic findings is discussed below; it is obvious that they are not those of pellagra.

A clinical diagnosis of possible biotin deficiency was entertained, but immediate attention was given to the urinary tract infection. Nevertheless, in spite of intensive

treatment with sulfathiazole, sulfanilamide and sulfapyridine, it did not clear up during the period of observation. On admission, the patient was placed on a regular hospital diet. Five days later this was supplemented daily

of avidin in raw egg whites. Therefore, on October 22 the patient was placed on a daily diet consisting of 1500 cc. of wine, the whites of twelve raw eggs, 1½ pounds of rare steak and coffee without cream or

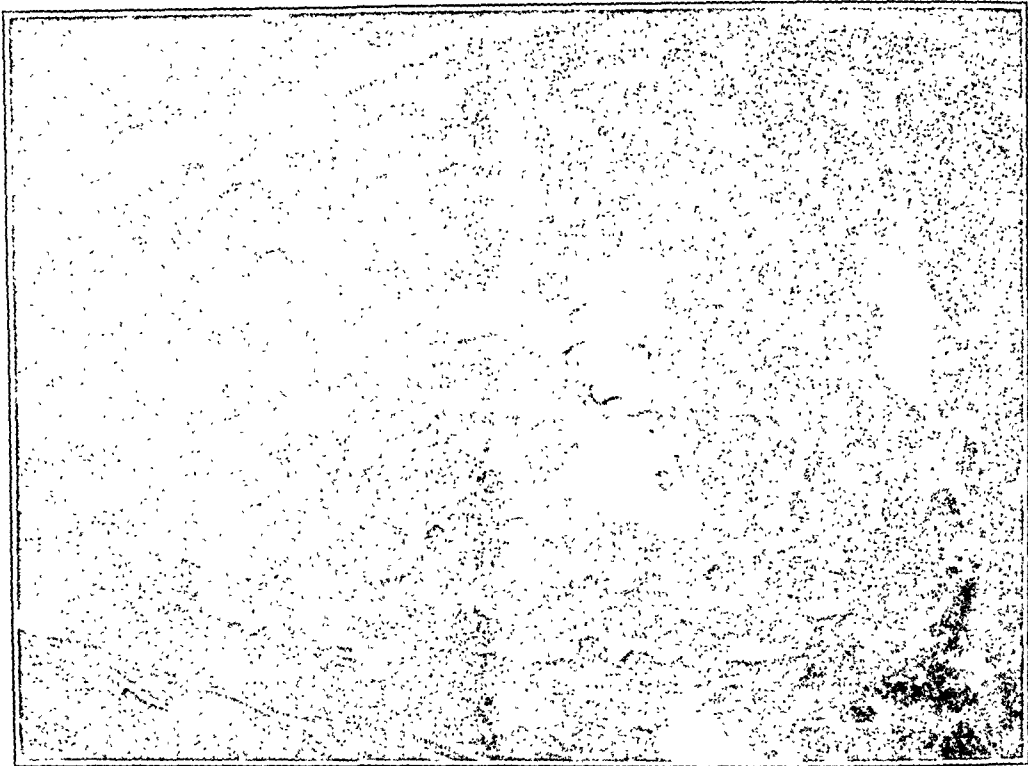


FIGURE 2. *Section of Skin.*
This shows the marked cellular reaction around the small blood vessels in the corium.

with 600 cc. of wine and three raw eggs. The quantities of these were increased until, a week after admission, he was eating, in addition to the hospital diet, six raw eggs daily in a quart of wine. Nevertheless, the rash

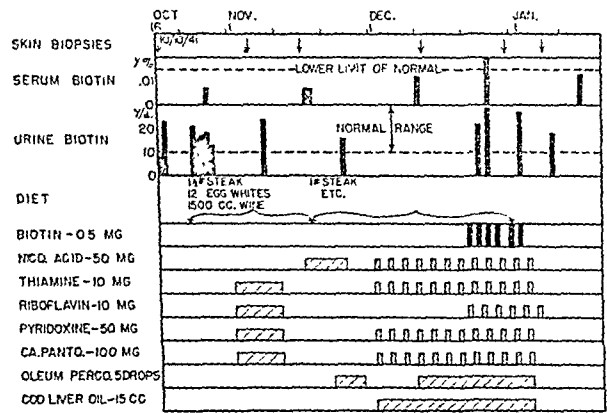


FIGURE 3. *Treatment Given the Patient and His Course in the Hospital.*

improved rapidly and by the end of 2 weeks there were only traces of it. Treatment of localized areas of the skin with ultraviolet and infrared light caused no exacerbation in the dermatitis. An attempt was then made to cause an exacerbation by limiting the biotin intake and giving a large quantity

sugar. All the wine issued had been made by the patient and contained 0.55 gamma of biotin per 100 cc. Therefore the daily intake of biotin in the form of wine amounted to approximately 8 gamma. Assays of the beef muscle were not performed.* The whites of twelve eggs contain a sufficient quantity of avidin to bind approximately 230 gamma of biotin.²⁷ Therefore, it seems that little if any biotin would be absorbed from the gastrointestinal tract. On some days, indicated in Figure 3, the diet was supplemented with 10 mg. each of thiamin chloride and riboflavin,† 50 mg. each of nicotinic acid and pyridoxine,† 100 mg. of calcium pantothenate,† 5 drops of oleum percomorphum and 15 cc. of cod-liver oil. On November 16, the steak was reduced to 1 pound per day and the regimen continued until December 29, a total of 10 weeks. On December 20, the patient was given subcutaneously 0.5 mg. of the methyl ester of biotin.† This dose was repeated on alternate days until a total of six injections had been given. During the course of this treatment the biotin level of the serum was found to be normal for the first time. The amount of biotin excreted in the urine increased, but remained within normal limits.

*Rat muscle has been found to contain some biotin,^{23, 28} although small in quantity as compared with that in liver and yeast. Beef muscle in daily doses up to 7.5 gm. has been found not to cure egg-white disease in rats.²⁴ Indeed, in some cases it seemed actually to accentuate the disease.
†I am indebted to the Winthrop Chemical Company, Incorporated, New York City, for the supply of riboflavin (Flavaxin Niphanoid); to Merck and Company, Incorporated, Rahway, New Jersey, for the supply of pyridoxine (Hexabione) and calcium pantothenate; and to the S. M. A. Corporation, Chagrin Falls, Ohio, for the supply of the methyl ester of biotin.

The second biopsy of the skin, obtained on November 4, showed marked regression of the inflammatory reaction. The subsequent four biopsies at scattered intervals during the next 2 months were essentially alike, showing to a slight degree hyperkeratosis, atrophy of the epidermis, increased pigmentation of the basal cells, edema of the corium, perivascular infiltration with lymphocytes, prominence of arrectores pilorum muscles and absence of sebaceous glands. During this time, however, there were slight or no gross abnormalities of the skin.

During the hospital stay there was a loss of 10 pounds in weight, due partially to improvement in the congestive heart failure. During this period of observation, one of the left inguinal nodes became enlarged and quite firm. This was apparently due to neoplastic extension. During the period of hospitalization the patient's general state of health appeared good and no new manifestations of vitamin deficiency developed.

DISCUSSION

The presence of an exfoliative dermatitis of several years' duration in a patient with poor dietary habits and the absence of a history of exposure to toxic factors strongly suggest that the dermatitis was due to a nutritional deficiency. A deficiency in any one of the following five vitamins has been found to induce in animals the development of a scaly dermatitis: nicotinic acid, riboflavin, pantothenic acid, pyridoxin and biotin. Therefore, the clinical and histologic changes of these vitamin deficiencies must be considered in comparison with those listed in the patient above. It should be emphasized, however, that comparisons of changes in animals may not be applicable to human beings.

A nicotinic acid deficiency can readily be eliminated, since the dermatitis was more central than peripheral and the histologic changes were definitely not those of pellagra. Furthermore, there was no accentuation of the rash on treating the skin with large doses of ultraviolet light and there was no diarrhea, delirium, atrophy of the lingual papillae and so forth.

The skin changes of riboflavin deficiency, as described in rats, are milder than those observed in this case. They usually consist of small, whitish-yellow, dandruff-like flakes or scales; the formation of large scales and exfoliation is conspicuously absent.³⁴ Histologic studies show mild hyperkeratosis, only very slight exudation in the upper corium, a decrease in the follicles and increased activity of the sebaceous glands.¹¹ In this case there was a marked exudative reaction in the corium and disappearance of the sebaceous glands. Moreover, cheilosis and vascularization of the cornea were absent.³⁵

The histologic manifestations of pantothenic acid and pyridoxin deficiencies in animals tend to overlap. With the former, there is a scaly dermatosis and alopecia without acrodynia.³ There

is also graying of the hair, hemorrhagic necrosis, serous exudate around the eyes, a twitch or paralysis of the hind legs and myelin degeneration of the sciatic nerves and spinal cord. Histologic changes of the skin in pantothenic acid deficiency have not been clearly distinguished from those due to pyridoxine deficiency.

Animals deficient in pyridoxine have a scaly dermatosis that is most marked around the nose, mouth and distal ends of the extremities.³⁶ Some areas of the skin remain normal. The formation of abscesses is common. On histologic examination one notes marked hyperkeratosis, acanthosis and intercellular edema of the epidermis.^{11, 36, 37} The corium is also edematous and hyperemic and is diffusely infiltrated with lymphocytes, large mononuclear cells and, later in the disease, polymorphonuclear leukocytes. In the early stages the hair follicles and sebaceous glands remain intact, but in the late stages there is an infiltration of polymorphonuclear leukocytes into and around the hair follicles and sebaceous glands.

In animals with disease due to egg-white injury, there is acanthosis, parakeratosis, hyperkeratosis and intracellular and intercellular edema, without much cellular infiltration.³⁴

The changes that were noted in the sections of the skin of this patient were not entirely like any of the above-mentioned vitamin deficiencies. The picture was somewhat like that of biotin deficiency, but in addition there was a marked cellular reaction. The latter suggests the possibility of a pyridoxine deficiency, either alone or combined with biotin deficiency. The clinical picture, however, was not similar to the acrodynia of rats.

Thus, in summary, one may state that the macroscopic and microscopic changes of the skin of the patient were compatible with the diagnosis of biotin deficiency, but not pathognomonic of the condition as seen in animals.

Assays of the serum revealed that the biotin content was below the normal level. The first urine specimen was also low, but all subsequent ones were within normal limits (Fig. 3).

The ward diet during the first two weeks of hospitalization was perhaps sufficient in biotin content to account for the almost total disappearance of the rash. In spite of the fact that the patient was then placed on a dietary regimen permitting little or no absorption of biotin from the gastrointestinal tract, there was no exacerbation of the rash and the urinary excretion of biotin remained normal. The biotin content of the serum, however, stayed below normal. It seems that this apparently paradoxical situation can best be attributed to the persistence of the urinary-tract infection. It has been shown that many bacteria can

synthesize biotin. The colon bacillus and *Staph. aureus* can produce it in large quantities,³⁸ and these organisms were repeatedly present in the urine of the patient, although he had been treated with various sulfonamides. It is probable that some of the biotin synthesized in the kidneys was absorbed by the vascular system and distributed throughout the body.

Large doses of various members of the vitamin B complex, including biotin, did not cause complete disappearance of all the histologic changes in the skin.

If this case is correctly interpreted as one of biotin deficiency, it is of interest that the patient developed a carcinoma of the penis with progressive growth while in a state of biotin deficiency, because du Vigneaud et al.³⁹ have found that rats rendered biotin-deficient rarely develop carcinomas when fed butter yellow. Biotin was, however, regarded by them as exerting a procarcinogenic effect when butter yellow was fed to rats receiving a highly protective diet.

SUMMARY

A patient with an exfoliative dermatitis of several years' duration has been described. A long history of the ingestion of large quantities of raw eggs and of poor dietary regulation suggests that he had biotin deficiency.

Assays for biotin revealed that its content in the serum was persistently below normal, although it returned to normal on treatment with biotin. Most of the urine values were normal, possibly because of the persistence of a urinary-tract infection with biotin-producing organisms.

The dermatitis largely disappeared after the patient had been on a regular ward diet, without many raw eggs, for a period of two weeks.

Attempts to induce the reappearance of the dermatitis by the administration of a diet with large quantities of raw egg white and of low biotin content failed, possibly owing to the infection of the urinary tract.

The coexistence of a carcinoma is of interest in a patient with possible biotin deficiency.

I am indebted to Dr. Paul György, of the Babies' and Children's Hospital, Cleveland, Ohio, for his numerous helpful suggestions and the bioassays of the various specimens for biotin.

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MEDICAL PROGRESS

ENDOSCOPY*

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ENDOSCOPIC procedures are being used more and more frequently in all large clinics, where facilities for them are readily available. The clinician must know when to call on the specialist for the various endoscopies. It is hoped that the following review will help to indicate the trend of modern endoscopic thought and will assist the physician in deciding when the endoscopist should be called in consultation.

ANESTHESIA

In all the large endoscopic clinics local anesthesia is used almost entirely. In the clinic at the Massachusetts General Hospital 5 per cent Larocaine Hydrochloride or 2 per cent Pontocaine Hydrochloride has been substituted for cocaine, because although the latter may be somewhat more effective, it is probably more toxic than either Larocaine or Pontocaine. During the last few months it has been impossible to obtain Larocaine, and 2 per cent Pontocaine has been used entirely, without untoward results.

A reaction to Pontocaine, however, was reported by Phillips, Congleton and Tuttle.¹ Approximately 5 cc. of 0.5 and 1.0 per cent Pontocaine was used. Almost immediately there were fainting, twitching of the facial muscles and general tonic contractions, which were relieved by the intravenous administration of Dial. Other reactions to Pontocaine have been reported, but none to Larocaine.

BRONCHOSCOPY

Bronchiectasis. Blades and Graham² in a discussion of the surgical treatment of bilateral bronchiectasis mention that in some cases there has been difficulty in deciding from the appearance of lipiodol bronchograms which of the lungs was more extensively diseased. In these cases the impressions gained by bronchoscopic examinations were relied on to determine the major source of pus.

Diamond and Van Loon³ studied 75 cases of bronchiectasis in children from the point of view of bronchoscopic aspiration, and concluded that

most of the patients were subjectively improved by repeated bronchoscopies, but that in not a single case was there an anatomic cure.

Hemorrhage. In a study of 436 patients with hemoptysis, Jackson and Diamond⁴ found the commonest causes to be bronchiectasis (138 cases), carcinoma (82 cases), tracheobronchitis (74 cases), pulmonary abscess (51 cases), no evidence of disease (34 cases), nonsuppurative pneumonitis (15 cases), suppurative pneumonitis (11 cases) and adenoma (11 cases). Other rare diagnoses made up the balance of the series. The high percentage of tracheobronchitis is worthy of note, for many physicians do not seem to recognize this condition as a cause of hemoptysis. In all these cases x-ray examination of the chest was negative. Nine patients had had one or more massive hemoptyses.

Parrish⁵ reports 1 case of fatal hemoptysis in which bronchoscopy showed only a friable mucosa. This was confirmed by autopsy, which showed only erosions of the bronchial mucosa. This seems comparable to the cases of massive and even fatal hemorrhage from gastritis, and serves to emphasize the fact that serious hemorrhage does occur from badly inflamed mucous membranes with erosions but without actual ulcerations.

Asthma. Bases and Kurtin⁶ emphasize the importance of bronchoscopic aspiration in status asthmaticus. They report that 6 of the 7 patients who died of status asthmaticus at the Mount Sinai Hospital in the past fifteen years and on whom autopsies were performed died from blocking of the tracheobronchial airway by excessive outpouring of secretion. In many cases death could have been averted by bronchoscopic removal of the obstructing secretion.

Postoperative bronchoscopy. Schmidt, Mousel and Harrington⁷ stress the necessity of preventing atelectasis in the postoperative patient. In certain cases of bronchial obstruction they advise one or more bronchoscopic aspirations before operation to free the lung of as much of the infected secretion as possible.

Sealy and Priestley⁸ report a case of total gastrectomy and cholecystectomy at the same time with very smooth convalescence. They attributed this result to an immediate postoperative bron-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C. Thomas Company, 1942. \$5.00).

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choscopy during which a considerable amount of bloody debris was aspirated from both sides of the tracheobronchial tree, and believe that had this material not been aspirated, a pulmonary infection would in all likelihood have developed which would have interfered materially with the patient's convalescence. At the Massachusetts General Hospital we consider this of such significance that we are training our anesthetists in the use of the bronchoscope for postoperative aspiration of secretions.

Bird⁹ writes interestingly regarding the value of bronchoscopic aspiration immediately following operation. He reports that after the passage of an ordinary catheter through the endotracheal tube, one may still hear bizarre, coarse rales over various portions of the bronchial tree. If a bronchoscope is then introduced, exudate is always found, usually in small amounts, distributed irregularly along the sides of the trachea and large bronchi and in the orifices of some of the secondary bronchi. On removal of this bubbling fluid, on auscultation the lungs will be found entirely clear. Bird believes that removal of this residual, even though small, is essential, for if it remains it may cause localized bronchial infection and an exhausting, ineffective cough.

Carcinoma. Holleb and Angrist¹⁰ report 2 cases of bronchogenic carcinoma associated with pulmonary asbestosis. Although these cases are of interest, it is impossible to prove a causal relation between the two conditions.

Prickman, Maytum and Moersch¹¹ observed 3 cases of primary bronchogenic carcinoma in asthmatic patients. Here again the significance of chronic irritation in the development of carcinoma is of interest but no causal relation can be proved.

Ochsner and DeBakey¹² have made a careful study of metastases from primary carcinoma of the lung, and conclude that in this disease there is a high incidence of metastases at the time the diagnosis is made, although fortunately some cases of bronchogenic carcinoma are characterized by late and limited metastases. The relative incidence of metastases to various organs and lymph nodes based on a collected series of 3047 cases is presented.

Goldman¹³ made a special study of carcinoma of the lung of long duration. In a series of 11 selected cases, 10 of which were epidermoid, the duration from the time of onset of symptoms until diagnosis averaged ninety months. Goldman blames the delay in diagnosis on the inadequacy of bronchoscopy and roentgen examination to demonstrate early small peripheral tumors, particularly when complicated by empyema and abscess. *He urges the education of both patient and physi-*

cian "to produce in them an anaphylactic reaction" to the possibility of cancer in men over forty with symptoms of pulmonary disorder.

Adams, Steiner and Bloch¹⁴ discuss what they call malignant adenoma of the lung, or carcinoma-like tumors of several years' duration. They report 5 cases of endobronchial tumor characterized by a long clinical course with low-grade but definite malignant manifestations. I believe that in general it is possible for pathologists to differentiate benign from malignant tumors. The term "bronchial adenoma" should denote a benign tumor, and as a tumor becomes invasive it should be called a carcinoma. "Malignant adenoma" seems to be somewhat of a contradiction in terms.

Clerf and Bucher¹⁵ report 35 cases of adenoma of the bronchus in 243 consecutive cases of carcinoma, an incidence of 14 per cent. In one case an adenoma involved the trachea and both main bronchi. In another, an apparently benign adenoma was shown five years later to be a carcinoma; at post mortem there was a mass in the lung with metastatic carcinoma in the lymph glands of the mediastinum. When one considers the possibility of some adenomas' being relatively low-grade carcinoma, it is evident that lobectomy or pneumonectomy must be seriously considered, not only from the point of view of possible malignancy but also because, even in benign adenomas, there is frequently irreparable lung damage.

Tuberculosis. Brantigan, Hoffman and Proctor¹⁶ point out that the increasing use of bronchoscopy for tuberculous patients has revealed a significant percentage of pulmonary lesions to be complicated by endobronchial lesions. They advise routine bronchoscopies before the performance of pneumolysis.

Durkin and Vinson¹⁷ report the favorable outcome of a tuberculous bronchial stricture treated by high-voltage roentgen therapy. Since tracheobronchial tuberculosis may heal spontaneously, the value of x-ray therapy in this disease is easily exaggerated.

Phelps¹⁸ emphasizes the poor prognosis in tracheobronchial tuberculosis, having found 31 per cent of a series of patients dead in five years, 63 per cent with chronic disease and only 6 per cent completely recovered. He finds the local application of 30 per cent silver nitrate helpful.

Alexander, Sommer and Ehler¹⁹ are opposed to any form of collapse therapy for pulmonary tuberculosis when there are signs or symptoms of tracheobronchial tuberculosis until bronchoscopy has been performed to determine the type, position and extent of the bronchial lesions. After a long discussion, these authors conclude that there are certain clear-cut indications and contraindications

to both pneumonectomy and thoracoplasty in the treatment of pulmonary tuberculosis with bronchial stricture, atelectasis and fibrosis that must be strictly observed if a high percentage of therapeutic failures is to be avoided. In some cases neither pneumonectomy nor thoracoplasty can be used safely. For those cases in which no contraindication to either pneumonectomy or thoracoplasty exists, they believe that thoracoplasty is the better operation, because the mortality is much lower than with pneumonectomy and the percentage of apparent healing of the tuberculosis is much higher. Chamberlain and Gordon²⁰ consider the problem of endobronchial tuberculosis involving the large bronchi as essentially one of mechanical obstruction and its complications (emphysema, bronchiectasis, atelectasis and so forth). They also hold that early bronchoscopic recognition of the bronchial disease and reduction in the size of the pulmonary bed before chronic stenosis occurs are of fundamental importance in the therapeutic program; that pneumothorax is a dangerous form of therapy when the bronchial disease is severe and large bronchi are involved; that the local application of silver nitrate often aids therapy directed at the pulmonary lesion; and that severe endobronchial tuberculosis produces permanent damage to the bronchus and is accompanied by irreversible sequelae. *A permanent form of therapy is therefore indicated. The results from thoracoplasty have been good. External drainage, lobectomy and pneumonectomy may be used in selected cases.*

Thornton and Adams²¹ in an article on the resection of lung tissue for pulmonary tuberculosis conclude as follows: The commonest complications have been persistent fistula, contralateral spread and empyema. The commonest indications for operation have been tuberculoma and isolated tuberculous lesions simulating tumor, tuberculous bronchiectasis, bronchial stenosis and post-thoracoplasty cavities. The best results were obtained in patients with closed lesions or with negative sputums. Resection of lung tissue in cases with bronchial stenosis is suggested only if secretions cannot be made to drain past the stricture. Rarely lobectomy or pneumonectomy may be performed in this type of case in the presence of a positive sputum; in general, however, resection of lung tissue is hazardous in the presence of a positive sputum. If possible, collapse therapy is preferred.

Benedict²² in a symposium on bronchial obstruction discussed the problem of tracheobronchial tuberculosis. He emphasizes the fact that only by bronchoscopy can the differential diagnosis be established between this disease and other diseases

causing bronchial obstruction, especially benign and malignant tumors.

From this review of the literature it is apparent that the medical profession is becoming increasingly aware of the importance of bronchoscopy in tuberculosis.

ESOPHAGOSCOPY

Carcinoma. The most significant advance in surgery of the esophagus has been resection of lesions of the lower end by the transthoracic approach. Churchill and Sweet²³ have reported their experiences in this field and have described in detail the operative procedure whereby the tumor is resected and a direct anastomosis made between the esophagus and stomach. Esophagoscopy is essential for determining the nature and level of the lesion, and especially for procuring tissue for microscopic diagnosis. The results of operation compare favorably with those for resections for carcinoma in other locations of the stomach.

Carcinoma of the upper esophagus is notoriously difficult to treat, but Wookey²⁴ has described a method of surgical removal of such growths even when they involve the hypopharynx. Complete removal of the larynx and pharynx may be necessary, and in such cases it has been possible to reconstruct the pharynx and upper esophagus to permit the normal taking of food.

Benign tumors. Samson and Zelman²⁵ report that benign tumors are often asymptomatic and are encountered accidentally at autopsy. They are located predominantly in the upper fourth of the esophagus and include lipoma, myxoma and fibroma. In a series of 26 cases of grossly pedunculated tumors, 3 patients died suddenly because of regurgitation of the tumor into the larynx. After a thorough consideration of treatment by esophagotomy or esophagoscopy, it is the opinion of the authors that endoscopic removal is superior to extirpation by external esophagotomy.

Benign stricture. Certain cases of esophageal stricture have been found to be impenetrable. In such cases Drash and Woodward²⁶ recommend a surgical approach combined with the use of a bougie manipulated within the esophagus and manually from without.

Cardiospasm. Etzel²⁷ presents data which he believes tend to show that megacardiospasm (cardiospasm), megacolon, achalasia of the pylorus, megarectum and disturbances in the cardiac conduction system are but varied manifestations of the same disease. A chronic or intermittent deficiency of vitamin B₁ is suggested as the etiologic agent of the degeneration in the autonomic nervous system, thereby instituting a series of physiopathologic

changes that culminate in the clinical picture described.

Samson and Foree²⁸ have reviewed the literature on the injection treatment of esophageal varices and report 1 case in which sclerosis was obtained by nine injections of 0.5 to 6.0 cc. of 2.5 per cent sodium morrhuate. They believe that the method has merit and deserves further trial. In their case many varices were present in the stomach.

GASTROSCOPY

Taylor²⁹ has described a new gastroscope the flexible part of which can be curled up or allowed to lie flaccid. It is flexible in all directions, but can be bent forward and backward in the plane of the objective up to the limits of optical flexibility. By reason of this controllable flexibility the new instrument possesses the following advantages: greater safety of instrumentation, less likelihood of failure of instrumentation, abolition of blind areas in the stomach, ability to move the instrument about in the stomach so as to inspect any particular area closely at will and from more than one angle and greatly increased illumination with less distortion of the image. In fact, endoscopic photography, which has previously been impossible with other flexible gastroscopes, has now become practicable.

Gastritis. Barnett³⁰ studied the symptoms of superficial gastritis and found no correlation between the symptoms and the severity of the gastritis as seen through the gastroscope. He found frequent gastroscopic evidence of transition from superficial to atrophic gastritis.

Benedict³¹ in a series of 1300 cases examined by gastroscopy found hypertrophic gastritis without other gastric or duodenal disease in 117 cases (9 per cent). The commonest symptom was epigastric pain, which occurred in 74 per cent of the cases. It was relieved by food or soda in 81 per cent, related to meals in 52 per cent and present at night in 21 per cent. The similarity to ulcer pain is therefore striking. Other frequent symptoms were vomiting (45 per cent), hemorrhage (42 per cent), gas (41 per cent), sour eructations (16 per cent) and heartburn (15 per cent). Clinical improvement was in most cases definitely correlated with the improvement in the gastric mucosa as seen by gastroscopy. The expert roentgenologist using the relief technic may be helpful in suggesting a possible diagnosis of gastritis, but the only way of obtaining a positive diagnosis is by gastroscopy, and only by it can the differential diagnosis be made between the superficial, atrophic and hypertrophic forms. No method is wholly accurate in differentiating some severe cases of hypertrophic gastritis from those of carcinoma. In

doubtful cases surgical exploration, including gastrotomy and biopsy, should be performed.

Olleros³² points out that pernicious anemia is usually accompanied by atrophic gastritis, which may improve with liver therapy to a point where as observed through the gastroscope the lesion appears to be undergoing complete cure, although the improvement is never accompanied by histologic restoration. In tropical sprue Olleros found atrophic gastritis localized or generalized, but not so severe as that seen in pernicious anemia. After liver therapy the symptoms were checked and the gastroscopic characteristics ceased to predominate.

Einsel³³ reports a case of superficial ulcerative gastritis following tryparsamide therapy for syphilis. This patient had had heavy antisyphilitic treatment, which was followed by uncontrollable vomiting of several weeks' duration. Gastroscopy demonstrated hundreds of eroded areas, 2 to 4 mm. in diameter, with a pearly-white base and red edge. The mucosa was edematous and bled easily.

Judd³⁴ has carefully studied the residual lesions of ulcerative gastritis and their possible relation to the development of carcinoma of the stomach. In a review of the literature he emphasizes that cancer is always accompanied by gastritis (Faber³⁵); that cancer never develops in a healthy stomach (Hurst³⁶); that most carcinomas of the stomach probably arise on the basis of a chronic atrophic gastritis (Tuomikoski³⁷); that gastric carcinoma may follow the atrophic type of gastritis (Schindler, Ortmayer and Renshaw³⁸); and that the hyperplasia of the mucous glands may have some relation to the development of carcinoma (Robertson³⁹). Judd made a microscopic study of surgically resected stomachs, and found a consistently lower incidence and markedly less prominent degree of hyperplasia in the control groups than in the cancer group, lending support to the conclusion that hyperplasia or regenerative activity is an important factor in the pathogenesis of carcinoma of the stomach. His final conclusions are that carcinoma develops in a previously damaged stomach; that many years of such injury may be required before neoplastic transformation begins; and that the pathogenesis of gastric carcinoma is directly related to the disorganized hyperplasia of gastric mucous cells.

Benedict and Mallory⁴⁰ made a careful study of 51 cases of surgically resected stomachs in an attempt to correlate the gastroscopic with the pathological findings in gastritis. The correlation was found to be more accurate than had been expected, and confirms the accuracy of the gastroscope in the diagnosis of gastritis and the differentiation of the various types of gastritis. Superficial gastritis as described by the gastroscopist cor-

responds to the acute exudative gastritis of the pathologist. The term "atrophic gastritis" is used by both gastroscopist and pathologist to denote the same type of mucosa. Hypertrophic gastritis as described gastroscopically corresponds to an exaggerated form of the physiologic plasma-cell and lymphocytic infiltration of the normal stomach. In this series there was complete or partial agreement between the gastroscopist and the pathologist in 88 per cent of the cases.

Gastric ulcer. Wolf and Wolff⁴¹ studied the effect of emotions on the gastric mucosa of a patient with a gastric fistula, and found that intense sustained anxiety, hostility and resentment were accompanied by severe and prolonged engorgement, hypermotility and hypersecretion in the stomach. In this state mucosal erosions and hemorrhages were readily induced by even the most trifling traumas, and frequently bleeding points appeared spontaneously as a result of vigorous contractions of the stomach wall.

Carcinoma. Moersch and Weir⁴² present a case of prolapse of the gastric mucosa in which the lesion was misinterpreted gastroscopically as being gastric carcinoma. They believe that repeated gastroscopic examinations obviate such errors, and that palpation of the abdomen during gastroscopy aids the gastroscopist in determining the pliability of the gastric wall and in bringing into view portions of it that might otherwise not be visualized.

Templeton and Boyer⁴³ have analyzed the gastroscopic and roentgenologic findings in the diagnosis of gastric cancer, and conclude as follows: In most cases a gastric cancer visible by one of the two methods of examination is demonstrable by the other, and will be diagnosed correctly by both the gastroscopist and the roentgenologist. Sometimes a lesion, by virtue of its location and morphology, is visible only to the gastroscopist or to the roentgenologist. Occasionally, lesions that are demonstrable by both methods are diagnosed as malignant by one examiner and as benign by the other, and when the facts finally become known it is found that the gastroscopist is no more and no less likely than the roentgenologist to be correct. Lastly, a combination of gastroscopy and roentgenology will result in a higher percentage of correct diagnoses than will either procedure alone.

Benign tumor. Cohn, White and Weyrauch⁴⁴ report an interesting case of granuloma of the stomach which followed the ingestion of medication containing colloidal kaolin (hydrated aluminum silicate). The patient had had abdominal pain, pyrosis, nausea and vomiting for eight years. Clinical and roentgenologic examination revealed no gastric disease. Gastroscopy showed a prepyloric tumor, which, however, was not seen in the

grossly resected stomach. Microscopic study proved the lesion to be a granuloma with the type of foreign-body giant cell present in the lesions of silicosis. Mineralogic studies confirmed the presence of silica in the gastric tissues. Following resection the patient became asymptomatic and remained so for over two and a half years.

Schindler, Sandweiss and Mintz⁴⁵ state that it is possible to make a diagnosis by gastroscopy of a benign submucosal tumor by the stretching of a mucosal fold from the surrounding mucosa up to the surface of the tumor. The appearance of this type of tumor as seen by gastroscopy has also been illustrated by Benedict.⁴⁶

Seasickness. Schwab⁴⁷ studied 38 cases of chronic seasickness in naval personnel and found that the patients fell into two groups: those constitutionally sick, with a history of car, bus and other sickness and with poor efficiency at sea; and those with severe seasickness, without the history of other sicknesses ashore and with a fair degree of efficiency at sea. Unfortunately, gastroscopy was carried out in only 2 cases.

PERITONEOSCOPY

Beling⁴⁸ believes that peritoneoscopy has not received the attention to which it is entitled. He thinks that if its indications and contraindications were better understood, the correct use of the peritoneoscope would bring about more accuracy in diagnosis and more correct treatment. He states that peritoneoscopy is indicated for the following conditions: noninflammatory disease of any of the organs within the greater sac of the peritoneal cavity, excluding the contents and border of the lesser sac, the pancreas, the kidneys and other retroperitoneal structures, with certain exceptions; a pancreatic growth, particularly one interfering with the continuity of the common bile duct, or one suspected of metastasis; a retroperitoneal mass (for determination of the location of an intra-abdominal mass with relation to the peritoneum); a suspected neoplasm or anomaly of any of the pelvic organs, including endometriosis; old chronic inflammatory disease of any of the pelvic organs; suspected ectopic pregnancy; splenomegaly or hepatomegaly; ascites not of cardiac origin; and tuberculous peritonitis. He particularly emphasizes the importance of peritoneoscopy in determining the presence or absence of liver metastases, primary carcinoma of the liver, hepatic cirrhosis, pelvic malignancy and ascites.

Donaldson, Sanderlin and Harrell⁴⁹ report a method of suspending the uterus without open abdominal incision by using the peritoneoscope and a special needle. This appears to be an ingenious idea, and the procedure is no doubt prac-

licable in certain cases, but I am advised by gynecologists in this clinic that this type of suspension (Olshausen) is seldom used nowadays, and that therefore peritoneoscopic suspension would be infrequently indicated.

Hamilton⁵⁰ reports a new instrument consisting of a blunt-tipped rod with a "manipulator" and an insulated endothermy electrode, both of which fit into the sheath of a small paracentesis trocar through an airtight nipple. When needed, the trocar and sheath are introduced through a tiny separate stab wound under peritoneoscopic view, the trocar is removed, and the manipulating rod or electrode is inserted. The electrode is capable of dividing adhesions, opening benign cysts and so forth. With the rod, obstructions to peritoneoscopic vision are pushed aside or hidden structures are lifted into view. The author reports no accidents, and gratifying results.

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**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL**

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29081**PRESENTATION OF CASE**

A four-month-old girl was sent to the hospital because of fever, cough and extreme restlessness.

Three days prior to admission the patient developed a slight dry, hacking cough and seemed pale. She moaned all night, seemed feverish and became increasingly irritable. Her appetite was poor, but she took water well. At no time did she vomit. Bowel movements were normal. The child was treated at home with *Argyrol* nose drops and alcohol rubs.

The family history was negative. There was no evident exposure to contagion or illness of any kind. The child was delivered at term after a normal pregnancy. She was breast fed, and vitamin supplements were provided after three weeks of age. The child gained weight and seemed quite normal prior to the present illness.

Physical examination disclosed a well-developed and well-nourished but acutely ill child who was flushed but seemed well hydrated. Respirations were rapid and of a grunting type. There was no rash. The fontanelles were flat. Both eardrums were slightly congested, but the landmarks were normal. The nose was clean. The throat was slightly congested. Expansion of the chest was symmetrical. Over the entire lower part of the left lung the percussion note was impaired and bronchovesicular breathing was audible. Examination of the heart and abdomen was negative. The liver edge was palpable at the costal margin.

The temperature was 104°F.

Examination of the blood revealed a red-cell count of 4,200,000 with a hemoglobin of 105 per cent, and a white-cell count of 15,450 with 53 per cent polymorphonuclear leukocytes, 38 per cent lymphocytes and 9 per cent monocytes. A throat culture demonstrated a few beta-hemolytic streptococci.

An x-ray film of the chest showed an area of consolidation behind the heart in the left lower lobe. The left costophrenic angle was partially obliterated.

In spite of a course of sulfadiazine producing a blood level of 5.0 mg. per 100 cc. the child's tem-

perature remained elevated, spiking daily to over 104°F. On the second day after admission the right eardrum was acutely inflamed and bulging and the landmarks were obliterated. One observer believed that the signs of consolidation had spread to the left upper lobe and possibly to the right upper lobe. Marked abdominal distention developed, and the child died on the fourth day after admission, the temperature finally rising to 106.1°F and the respirations to 60.

DIFFERENTIAL DIAGNOSIS

DR. RALPH A. ROSS: The history in this patient is one of a mild respiratory infection gradually progressing without apparent fluctuation. The remark about the moaning of the child is of some interest since babies who are sick often have a sighing type of respiration that might be called moaning.

The examination at the time of admission gave evidence of bilateral otitis media shown by congestion of both eardrums and also of some type of consolidation in the left lower lobe. The red-cell count was normal. One wonders whether the hemoglobin reading of 105 per cent was accurate. It is a striking degree of hyperchromatism in the red cells for an infant of four months; in the newborn period, of course, it is regularly seen. The leukocytosis is perfectly compatible with an acute infection in a child of this age. The relatively high percentage of monocytes does not point in any one direction.

The most important laboratory finding is the throat swab; even a few colonies of beta-hemolytic streptococcus in an infant of four months are of possible pathologic significance. However, it is generally understood that throat cultures are not indicative of the true etiologic agent in the lower respiratory tract; one should make a nasopharyngeal culture or one from material coughed up from the lower respiratory tract. To obtain the latter is a difficult procedure, which takes some degree of experience. The former can be easily carried out with the proper equipment. One wonders about blood cultures. There is no mention of them.

I should like to see the x-ray films.

DR. GEORGE W. HOLMES: The process spoken of in the chest is visible at this point, close to the angle of the diaphragm and the spine, and is more or less hidden by the shadow of the heart. There is also an area out toward the periphery that obscures the angle between the diaphragm and the chest wall, which may be a continuation of the same process. The diaphragm is not elevated. There is no evidence of decreased aeration in the lung. One would not seriously consider a plug-

ging of the bronchus, with a collapsed lung. It looks more like consolidation of some sort.

DR. ROSS: There is no evidence of fluid?

DR. HOLMES: No.

DR. ROSS: The clinical picture, together with the laboratory evidence, is one of a generalized respiratory infection involving the throat and ears and producing a localized pneumonic process. One is tempted to incriminate the hemolytic streptococcus as the etiologic agent, inasmuch as that organism was found in the throat. However, hemolytic streptococci may be found at the same time that other pathogenic organisms are present in the lower or upper respiratory tract and may not be the real cause of the difficulty. In this age group, under six months, pneumonia is still a serious problem. Before the advent of chemotherapy the fatality rates in this age group were as high as those at the other extreme of life. Some figures show up to 40 or 50 per cent mortality.

Thus we have a patient who was, by reason of her age, unable to handle the type of infection that we suppose was present. Lack of adequate response of the patient to infection often leads to the accumulation of purulent material, either because of infection of the serous cavities or because of a breaking down of the involved portion of the respiratory tract.

In the hospital course there was a steady progression downhill, with a spiking temperature and the probable spread of the pneumonia. The question of fluid in the pleural cavity comes to mind as the cause of spread of signs in the chest, but we have no further evidence of that. The appearance of otitis media of a purulent type indicates a progression of the process. One wonders whether we are justified in saying it was justifiable to state that the temperature remained elevated "in spite of a course of sulfadiazine producing a blood level of 5 mg. per 100 cc." Five milligrams is considered the lower limit of the effective level of sulfadiazine, and, particularly in this age group, a higher level should be aimed at. The development of distention in the last forty-eight hours of life may have been entirely on the basis of paralytic ileus, which is frequently seen in serious pneumonia. On the other hand it may have been due to the spread of the infection to the peritoneum.

The diagnoses are localized pneumonia, purulent otitis media on the right and a purulent intrathoracic complication — empyema or a breakdown of the involved lung into multiple abscesses. Peritonitis is a remote possibility.

DR. ALLAN M. BUTLER: Another point that this case brings to mind is the necessity today of trying to be specific in the bacterial diagnosis of a severe respiratory infection, whether it is tracheitis,

bronchitis or pneumonia. One wonders if all of us at times have been a little too satisfied with just giving sulfonamide therapy in such cases without tracking down the specific etiologic agent. The reason it is important is that we have specific therapy for certain types of infection. For instance, with influenzal infection we have specific anti-influenzal rabbit serum that should be given in conjunction with chemotherapy. If Dr. Castleman should say in a moment that the cause of infection in this child was a staphylococcus and not a beta-hemolytic streptococcus, then, with penicillin available, the specific therapy should be a combination of penicillin and sulfadiazine. The search for the specific infectious agent should be pursued with just as much intensity now as it was prior to the days of sulfonamide therapy.

DR. BENJAMIN CASTLEMAN: How would you go about it?

DR. BUTLER: In this particular case, every effort should have been made to get nasopharyngeal cultures, which are better than throat cultures. With the spike in temperature, blood cultures should have been obtained. I imagine such efforts were made but were not successful.

DR. CASTLEMAN: A blood culture was taken but did not grow out by the time the patient died.

CLINICAL DIAGNOSES

Bronchopneumonia.
Bilateral otitis media.

DR. ROSS'S DIAGNOSES

Pneumonia, localized.
Otitis media, purulent, right.
Intrathoracic purulent complication (empyema or multiple abscesses).

ANATOMICAL DIAGNOSES

Pulmonary abscesses, multiple, left.
Empyema, left.
Bronchopneumonia, left.
Otitis media, acute, bilateral.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this child showed an empyema in the left pleural cavity, which was filled with thick creamy-yellow purulent material. The visceral pleura of that lung was studded with small abscesses 1 or 2 mm. in diameter. A cross section of the lung showed that the parenchyma itself was diffusely involved with abscesses 2 or 3 mm. in diameter. The intervening lung tissue was consolidated. The process probably began as a pneumonia and then rapidly broke down into small abscesses. A culture of the middle ears, both of which contained pus,

showed *Staphylococcus aureus*. I think therefore that we can be quite certain that the whole process was due to a staphylococcal infection, although the blood culture, even after a period of two weeks, showed no growth.

DR CHARLES JANEWAY: Was there a culture from the empyema cavity?

DR CASTLEMAN: One was taken but we could not find the report, I am sure that it was due to a staphylococcus. The fluid was thick and purulent, not the type one sees with a hemolytic streptococcus. There was no evidence of infection anywhere else including the sinuses of the head.

DR HOLMES: What was the date of death?

DR CASTLEMAN: Four days after the films were taken.

DR HOLMES: Do you think it would be possible for empyema to develop after these films were taken?

DR CASTLEMAN: Yes. There probably was some pleurisy at the time the films were taken, but probably little if any fluid.

DR JANEWAY: I should like to emphasize the fact that this was a staphylococcal case and that bacteriology of the respiratory tract should not be done in the conventional way, particularly when dealing with infants or children. Our tendency is to type a sputum for pneumococci and not even culture it. We are gradually getting away from that, but bacteriologists are prone to look at a plate only for hemolytic streptococcus and pneumococcus. If they do not see them they say that there are no important organisms. In the influenza epidemic two years ago, when staphylococcal pneumonia was a complication, we missed one or two cases until we became aware of the fact that on the blood plate made from the sputum the staphylococcus was by far the predominant organism. That is true in any severe infection of the respiratory tract in an adult when there is a virus infection or when there is trauma, such as occurs from the inhalation of smoke or poison gases, both of which give the way for secondary bacterial invasion. In the infant susceptibility is so great that no antecedent damage is necessary to enable the less pathogenic microorganisms to invade the lungs.

CASE 29082

PRESENTATION OF CASE

A sixty-two year-old blind housewife was sent to the hospital because of pain in the right foot.

Five years prior to admission the patient was said to have dropped a flatiron on her right foot. Three months before entry she noticed a constant

dull nonradiating pain in the lateral aspect of the foot, which became progressively worse. Approximately a month later swelling developed over the dorsolateral aspect of this foot, particularly after standing.

Her husband and a daughter were living and well. Sixteen years before admission the patient was treated for a gonococcal ophthalmia that produced bilateral corneal opacities and blindness. She denied venereal disease. For several years the patient had suffered from a loose cough, which was never productive of sputum. At no time had she had fever, chills, night sweats or hemoptysis.

Physical examination disclosed an obese woman in no distress who looked older than her stated years. Both corners were opaque. Medium coarse rales were audible posteriorly at the bases of both lungs. Examination of the heart and abdomen was negative. There was a firm, tender swelling of the right foot in the region of the fifth metatarsal bone. The mass could not be moved, did not pulsate and seemed to be attached to the underlying structures. The skin over the involved area was not red or edematous.

The blood pressure was 160 systolic, 85 diastolic. The temperature was 98.6°F, pulse 71, and the respirations 24.

The examination of the blood revealed a red cell count of 4,490,000 with a hemoglobin of 75 per cent, and a white cell count of 9000, with 33 per cent polymorphonuclear leukocytes, 20 per cent large lymphocytes, 33 per cent small lymphocytes, 10 per cent monocytes, 2 per cent basophils, 1 per cent eosinophils and 1 per cent unclassified cells. There was a moderate achromia of the red cells, and the platelets were slightly reduced. The urine was acid in reaction, had a specific gravity of 1.014 and showed a ++ test for albumin; the sediment contained 7 red cells, 50 white cells and 4 epithelial cells per high power field. The blood Hinton test was negative. The tuberculin test, employing a 1:1000 dilution of OT, was markedly positive.

An x-ray film of the right foot was unusual. The medial two thirds of the shaft of the fifth metatarsal bone showed osteophyte formation and short spicules of calcification extending laterally and inferiorly. The bone was decalcified proximally. Close to the distal head in the medulla there was a dense area of calcification within a radiolucent area. The metatarsal bone was increased in size. There was calcification of the blood vessels and local soft tissue swelling. A chest plate demonstrated calcified areas in the right upper lung just below the clavicle that were consistent with an old tuberculous lesion; there was no evidence of active disease. The lungs were otherwise clear. The heart was not remarkable.

Two days after admission a small fluctuant area developed on the lateral aspect of the right foot in the area of swelling. A small amount of serosanguineous fluid was aspirated, and this was negative for any specific organism, both on smear and culture.

An operation was performed on the eighth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. WALLACE: May I see the x-ray films?

DR. RICHARD SCHATZKI: I should describe this as cystlike destruction in the proximal half of the fifth metatarsal. The cortex is broken through in places, and there is coarse new-bone formation, which is perpendicular to the direction of the bone. The rays of new bone are thicker than those that one usually sees in osteogenic sarcoma. There is also soft-tissue swelling, and a localized area of increased density in the distal portion of the involved metatarsal that looks like an osteochondroma.

DR. WALLACE: Is there a fracture in the bone?

DR. SCHATZKI: No fracture is visible. There may well be one in that area, but the cortex is gone and no definite fracture is visible.

DR. WALLACE: The other bones are negative. Is there evidence of metastatic disease in the chest?

DR. SCHATZKI: No.

DR. WALLACE: The x-ray films are not helpful. We have a woman in her sixties with pain in the right foot of three months' duration and x-ray findings of a cystlike destructive lesion. Can this be a manifestation of some metabolic disease, such as parathyroidism? There is no other evidence for that. Just as a passing thought I shall mention gout. The x-ray films do not suggest it, and there were no tophi or other suggestive findings.

Could this be a syphilitic lesion? She is said to have had gonococcal ophthalmia. However, the patient denied venereal disease in its usual form, and the single blood Hinton test was reported to be negative. I believe that with a queer lesion of this sort, even with one negative Hinton test, we should continue to bear in mind syphilis as a possibility. Certainly the lesion is not characteristic.

Could this be a manifestation of sarcoid, with a lesion in the single bone? She is said to have had a negative chest plate.

DR. SCHATZKI: The chest plate is negative for metastatic disease. There is evidence of old tuberculosis.

DR. WALLACE: That rules out sarcoid. Xanthoma is a possibility, but multiple bones are usually involved.

The pain followed by swelling is suggestive of fracture. There is no story of recent trauma but if there had been a fracture it would have been a pathologic fracture. I am not sure that we can rule it out even by looking at the x-ray films. A fracture might account for some of the new-bone formation.

She had a normal temperature and white-cell count; in addition, some serosanguineous fluid was aspirated that contained no organisms on smear or culture. We should be able to rule out osteomyelitis on the basis of these findings. There may have been metastatic disease in this area, but again that is unlikely. It would be difficult to explain the x-ray findings on the basis of metastatic disease alone, because in general such lesions show punched-out areas of destruction of bone without new-bone formation.

Could this have been due to a tumor of the lymphoma series? Since there is no mention of nodes in general, we must assume they were not large enough to have come to anyone's attention. In considering the lymphoma series our attention is called to the differential count, which had a high proportion of lymphocytes. That does not establish the diagnosis, however.

Could this have been a benign bone cyst not related to a general disease? They are usually solitary and are not of common occurrence in this location. The question of chondroma also comes up. The increased density, as Dr. Schatzki said, is suggestive of a localized chondroma. That appearance could also be caused by multiple chondromas.

With bone proliferation we should think of Ewing's sarcoma, although, of course, the x-ray picture is not characteristic. The localized areas of bone proliferation with ray formation are suggestive of osteogenic sarcoma. Only one small area, however, looks like the ray formation that we so frequently see.

There is considerable evidence that this patient has had and perhaps has active tuberculosis. There were definite x-ray signs of healed tuberculosis. The white-cell and differential counts were, I believe, consistent with that disease, and she had a markedly positive tuberculin test with a dilution of 1:1000. Tuberculosis of bone is generally a destructive lesion and usually has its origin in the region of the joints rather than in the shaft of the bone, as appears to be the case here; however, I do not believe that we can rule it out.

Since this lesion is characteristic of nothing and I must speculate about it, and since there is more

evidence for tuberculosis than for anything else I shall make that diagnosis, with the reservation that it may have been one of a good number of lesions

DR TRACY B. MALLORY: Dr Schatzki would you like to express a further opinion?

DR SCHATZKI: I remember that we were puzzled by the case. The ray formation was a little similar to what we had seen in low grade infection. I do not remember what the final outcome was, so I am quite unbiased. I believe that the visible osteochondroma is significant and that the lesion turned out to be malignant tumor of bone, at least that is what I should call it now.

DR CHANNING C. SIMMONS: Dr Wallace has covered the possibilities well. In considering bone diseases, I like to divide them into four groups: generalized skeletal diseases, such as parathyroid disease and lymphoma; inflammatory diseases, such as syphilis, tuberculosis and osteomyelitis; primary bone tumors; and secondary or metastatic bone tumors.

Sarcoma is practically unknown in people over fifty, except in the presence of Paget's disease, and benign bone tumors are painless. Therefore I think primary bone tumors can be ruled out. A generalized skeletal disease can be excluded by the general examination. Metastatic tumors usually do not give this picture but can look like anything, just as lymphoma of the bone can simulate any other disease. My inclination is to consider this an inflammatory condition, possibly tuberculosis on the strength of the lung condition. The x-ray picture is not characteristic of any particular disease. The facts that she had pain and that fluid was obtained on tap, together with the high lymphocyte count, also suggest tuberculosis. One would have to repeat the blood Hinton test several times before syphilis could be excluded.

DR MALLORY: Three opinions were expressed on the ward. Chronic osteomyelitis was put down

as the first choice, the second was tuberculosis, and the third was bone tumor, type unclassified.

CLINICAL DIAGNOSIS

Chronic osteomyelitis

DR WALLACE'S DIAGNOSIS

Tuberculosis of metatarsal

A TYPICAL DIAGNOSIS

Chondrosarcoma of metatarsal

PATHOLOGICAL DISCUSSION

DR MALLORY: The lesion was explored, and a destructive process was found in the metatarsal. Some material was curetted out, which on frozen section a chondromatous structure following that the entire metatarsal was involved. The final histologic diagnosis was a low grade chondrosarcoma of the metatarsal.

It is difficult to draw a dividing line microscopically between benign and malignant tumors of bone.

Tumors that can behave in malignant fashion often look benign under the microscope. The one was sufficiently atypical so that I thought it to be called malignant. Moreover, it had destroyed the cortex and we found some small masses of cartilaginous tissue in the soft parts around the bone.

The wound was closed, and the patient was allowed to go home. She is returning to the hospital from time to time for observation. As yet no one has seriously raised the question of amputation although that is still under consideration.

DR SCHATZKI: Was there any infection present? If not, the x-ray picture rules out benign tumor.

DR MALLORY: The tumor had definitely destroyed the cortex.

DR SIMMONS: I should rule out benign tumor on the mere fact that the patient had pain.

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in England, particularly through the latter's Mental Health Emergency Committee. Total disbursements for 1942 for all purposes totaled nearly \$2,000,000.

The loss of key investigators, especially those engaged in clinical research, to the military and naval services has necessarily forced the curtailment or suspension of some projects, but the Commonwealth Fund has carried on with vigor its multifarious activities in medical education, rural hospitals and public health. A grant was made to the Long Island College of Medicine to pay for visiting instructors from other medical schools; ten fellowships for advanced study were awarded to junior instructors and staff members of medical schools and teaching hospitals. At several colleges the Fund subsidized special teaching units to acquaint pediatricians with the psychologic needs of sick children. Fifteen fellowships were offered to physicians and public-health workers from Latin American countries for postgraduate study in the United States. The outstanding research activities last year were related to respiration, renal function, the control of infectious diseases in armies, the epidemiology of poliomyelitis and the hereditary factors in the incidence of rheumatic fever.

The Commonwealth Fund has every reason to be proud of its solution of the problem of contributing fully to the war effort without the sacrifice of gains already made in nonmilitary fields. In short, it continues to carry forward, in war as in peace, the high purposes of its founder.

MEDICAL EPONYM

STOKES'S COLLAR

William Stokes (1804-1878) first described this phenomenon in the *Dublin Journal of Medical and Chemical Sciences* (5:400-440, 1834), in an article entitled "Researches on the Diagnosis and Pathology of Aneurysm." He discusses a case of aneurysm of the aorta as follows:

I was at once struck with the peculiar appearance of the neck. This was generally enlarged (giving the idea of the patient's wearing a collar or tippet), the jugular veins were turgid and tortuous.

He also mentions the phenomenon in the first part of *A Treatise on the Diagnosis and Treatment of Diseases of the Chest* (Dublin, 1837 — page 231) and again in *The Diseases of the Heart and the Aorta* (Dublin, 1854 — page 573), as follows:

As an indication of intrathoracic tumor, an extremely varicose state of the superficial veins of the neck and thorax is probably less frequent in aneurismal than in cancerous diseases. The pressure may be exercised on the venae innominae or the superior cava. . . . In other cases we find that in place of the large tortuous veins ramifying on the surface, there is a puffy elastic swelling of the entire neck. To this may be given the name of tippet-like swelling of the neck.

R. W. B.

RESOLUTION ON DEATH OF JOHN JOSEPH LUCY

Dr. John J. Lucy, late assistant visiting surgeon on the Second Surgical Service of the Boston City Hospital, died on December 28, 1942, in his forty-eighth year. He had been ill only about two months. He was born in Boston, and was graduated from Boston College and from Harvard Medical School. He took a surgical houseofficership at the Boston City Hospital, followed by a houseofficership at the Boston Lying-in Hospital. He was appointed to the Surgical Staff of the Boston City Hospital in 1925, having had the rank of assistant visiting surgeon for some years prior to his death. He was a member of the Surgical Staff of the Cambridge Hospital, being chief of one of the surgical services at that institution at the time of his death. He was a member of the American Medical Association, the Massachusetts Medical Society, the American College of Surgeons and the Boston Surgical Society, and for many years conducted a large private surgical practice.

He married Miss Alice L. McManus; this marriage was an exceedingly happy one, being blessed with seven children: four daughters and three sons, all of whom are living. In addition to his widow and children he is also survived by his mother.

Doctor Lucy was a man of real character, possessing the highest of principles, both professionally and personally. Loyalty was one of his outstanding qualities. In addition, he was endowed with a natural sympathy and understanding which endeared him to his fellow physicians, to his patients and to his friends. His loss to the profession and the community is indeed a great one.

BE IT RESOLVED, That in the death of Doctor Lucy the Staff of the Boston City Hospital has lost one of its most capable and conscientious members; and

BE IT RESOLVED, That the Staff of the Boston City Hospital express its most sincere sympathy to the family of Doctor Lucy; and

BE IT FURTHER RESOLVED, That these resolutions be placed upon the records of the Boston City Hospital and that the secretary be directed to send a copy to the family of Doctor Lucy and a copy to the *New England Journal of Medicine*.

WILLIAM P. BOARDMAN, *Secretary*
Executive Committee, Senior Staff
Boston City Hospital

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

IMPRESSIONS CONCERNING THE MATERNAL MORTALITY STUDY FROM 1937 TO 1941

The maternal-mortality study that the Section of Obstetrics and Gynecology of the Massachusetts Medical Society has carried on for the State Department of Public Health has been concluded. In some respects it is the most laudable study of this kind that has ever been carried on in the United States.

Many inquiries have been made concerning how this study was conducted. The start is the death certificate, which is signed by the physician and gives the cause of death. In Massachusetts the certificate is then taken to the office of the board of health of the town or city in which the death occurred and is then recorded and filed by the town or city clerk. According to regulations, a copy of each certificate should be filed at the office of the Secretary of State by the tenth of the month following the death; however, in some communities where there are few deaths the copies of the certificates are sent to the State House only at infrequent intervals. Each certificate that reaches the office of the Secretary of State is reviewed by a lay person, and the necessary corrections are made. Before it is filed it is coded by a lay person according to the international classification of deaths, and all deaths occurring within ninety days of childbirth are automatically classified as maternal deaths. All such deaths are reviewed by an investigator from the Department of Public Health, who is a registered physician. He makes a copy of each certificate covering a maternal death on a questionnaire prepared by the Children's Bureau of the United States Department of Labor, the front page of which has a replica of the death certificate. During the period of study, copies of these questionnaires were sent to the committee of the Massachusetts Medical Society. The com-

mittee in turn forwarded them to members of the Society in different parts of the State who were doing obstetrics, so that personal interviews with the physicians signing the death certificates might be held. It was hoped that these questionnaires might reach the investigators within, at most, two months of the day of death so that the interviews might be held when the facts were fairly clear in the minds of the attending physicians. In many cases, however, it was impossible to have these deaths investigated as soon as it was hoped they could be. Some certificates were filed at the State House many months after the death. Often by the time the investigator approached the physician whose name was on the certificate, it was found that the physician had left to join the armed forces, so that a personal interview was impossible. Some of the investigators were so busy with their work and the work of others that months elapsed before investigations were started. After the cases had been investigated, the reports were returned to the committee and formed the basis for the figures that have appeared in the *Journal*.

The mechanism of the study was not perfect, but as has already been said, the results are probably as good, if not better, than those obtained in any part of this country. A much more ideal set-up would be to appoint an obstetrician, either a young or an older man with plenty of time on his hands, who could personally investigate each death, irrespective of in what part of the state it occurred, within two months of the date of the death. This investigator with a committee of five should go over the cases and allocate them to such headings as were agreed on by all. In the present study the allocation of the cause of death was done by one obstetrician. Had the cases been gone over by a committee it is quite possible that some of the doubtful cases would have been classified differently. If one man with plenty of time on his hands were to conduct such an investigation he could inquire into many details that were not taken into consideration in the present investigation. Frequently a record was not so valuable as it might have been because no mention was made of the duration of pregnancy. Often no mention was made whether a living child was obtained. Circumstances, perhaps beyond the control of anyone, frequently led to records that were lacking in essential information. Such an investigation as this is no stronger than its weakest link.

The study has brought out several facts that show the weakness of the system and the inaccuracy of the figures. So long as it is the policy to include every fatality occurring within ninety days of childbirth as a maternal death, these sta-

tistics, from the point of view of obstetrics, will obviously be misleading. They will show the actual number of mothers who died, but among that number will be many whose deaths had nothing to do with obstetrics. For the figures to mean what they should, patients who die within ninety days of childbirth and whose deaths are found to be nonobstetric should be eliminated. An example of this is a patient who died of asthma brought on by allergy to aspirin.

In Massachusetts, it is perfectly possible, although commonly unrecognized, to change the cause of death on the original certificate when it is proved to be untrue. This may be done by the physician who signed the certificate provided he is able to present proof of its inaccuracy. This flaw in the vital statistics applies to all branches of medicine and surgery. Not infrequently, a patient who dies in a hospital has as the cause of death on the certificate a diagnosis that has been proved by autopsy to be incorrect. If the institution in which this death occurred made application to the office of the Secretary of State, the incorrect certificate could easily be rectified. Such a routine procedure would make vital statistics in Massachusetts more accurate than they are at present. This can and should be done.

In this state, all sudden deaths and those with a questionable cause must be referred to the medical examiner before the body may be buried. Since the medical examiner in the course of a year sees a number of maternal deaths, by applying to the district attorney for permission to perform an autopsy in cases in which the exact cause of death is unknown, he would be able to make an exact anatomical diagnosis. If this were done more frequently than it is, the statistics would be improved.

Another cause of inaccuracy is the fact that an incorrect diagnosis is sometimes written on the death certificate. This is partly due to ignorance, and partly to sentiment. An embolus, in the lay mind, has long been looked on as an act of God. "Hemorrhage and shock" are not pleasant terms to convey to the stricken family. It is gratifying that fewer questionable causes of death were found as the study progressed.

It is not fair to attribute all the improvement in the rate of the maternal mortality in Massachusetts during the past five years to this study. Nevertheless, the study has brought obstetrics into the open, and has made physicians conscious that their work is under scrutiny. The diminution in the number of maternal deaths in which bungling obstetrics played a part shows either that physicians are more expert or that they are more careful. At the beginning of the study, some of the doctors

resented an interview, since they believed that their privacy was being violated; this attitude no longer exists. Toward the end of the study, the co-operation between the general practitioner and the investigators was excellent. This study has also made the trustees of hospitals conscious of their responsibilities. They have at last learned to appreciate that their obligations to patients in hospitals extend to the medical care of those patients, and, in some instances, they have insisted that the practice of obstetrics should be supervised and that abnormal cases should be handled only by trained men. This achievement alone has made the study worth while.

The study has also brought out the fact that many women, either through ignorance or through stubbornness, do not receive adequate prenatal care. This is deplorable and warrants intensive educational propaganda.

In conclusion, the committee expresses its thanks for the co-operation that the physicians of Massachusetts have shown. It also expresses its deep appreciation for the willingness of those physicians who have served as investigators in these cases; the facts that they gathered, often under burdensome circumstances, have made the study possible.

* * *

The above paragraphs conclude the series of articles on the causes of maternal death that have been carried weekly in the *Journal* for the past four and a half months.

In the March 11 issue of the *Journal*, the Committee on Maternal Welfare will begin the presentation of a series of cases at two-week intervals. Half of these will concern instructive obstetric cases, and half will illustrate the proper handling of interesting and unusual neonatal cases.

DEATH

LEONARD — EDWARD J. LEONARD, M.D., of Dorchester, died February 15. He was in his forty-second year.

A native of Dorchester, Dr. Leonard received his degree from Georgetown Medical School in 1936. He had an internship at Mercy Hospital, Baltimore. He served on the staffs of the Carney Hospital and St. Margaret's Hospital. He was a member of the Massachusetts Medical Society, the American Medical Association and the Dorchester Medical Society.

His widow, four children, two sisters and two brothers survive him.

WAR ACTIVITIES

CIVILIAN DEFENSE

NURSING EXECUTIVES FOR EMERGENCY BASE HOSPITALS

To ensure adequate supervision of nursing service in emergency base hospitals, Surgeon General Parran of the United States Public Health Service has authorized the

appointment of a limited number of nurses with supervisory and administrative experience to serve as nursing executives, according to a recent announcement by the Medical Division of the United States Office of Civilian Defense.

Emergency base hospitals are institutions in relatively safe areas, adjacent to probable target areas, designated by the Medical Division to receive civilian casualties or other hospitalized persons from casualty receiving hospitals in the event of a grave wartime emergency.

The appointment of these nursing executives will follow in general the method that is being used in the appointment of physicians who, as members of affiliated hospital units, will hold inactive reserve commissions in the United States Public Health Service and will be called to active duty in emergency base hospitals only when additional staff is needed because of a war emergency.

Nurses recruited under this program may be assigned by the state chief of Emergency Medical Service to serve at emergency base hospitals either individually or with affiliated units. They may supervise a newly created nursing service or supplement the existing supervisory staff of an institution.

The nurses will be offered appointments in the United States Public Health Service as consultants on an inactive status and will be called to active duty by the Surgeon General on the recommendation of the state chiefs of Emergency Medical Service and regional medical officers only if their services are required at emergency base hospitals because of a military necessity, the circular states. When on duty they will be entitled to payment by the United States Public Health Service according to their experience and qualifications.

The circular authorizes the number of nurses to be recruited in each state for this purpose to be twice the number of affiliated hospital units actually being formed in the state. Although their appointments will obligate them to serve in an emergency base hospital in their regions if called to duty by the Surgeon General in a wartime emergency, they may resign their appointments at any time to accept assignments in the Army or Navy.

MISCELLANY

AMERICAN COLLEGE OF SURGEONS

New developments in military and civilian medical and hospital service will be brought to members of the medical profession at large and to hospital representatives through a series of twenty War Sessions, beginning March 1, to be held throughout the United States under the sponsorship of the American College of Surgeons with the co-operation of other medical organizations and of the Federal medical services.

Each session will consist of an all-day program, lasting from 9:00 a.m. to 10:00 p.m., including luncheon and dinner conferences. There will be eight meetings in each session, four of which will be for the entire assembly; the remainder will be divided into two meetings each for physicians and for hospital representatives. Subjects will be changed in the different states and service commands. Nationally known representatives of the United States Army, the United States Navy, the United States Office of Civilian Defense, the United States Procurement and Assignment Service and the United States Public Health Service will address the meetings and will lead the dis-

cussions, in addition to participation by prominent leaders in civilian medical practice and hospital service.

The topics relating to military medicine to be discussed will include care of the ill and injured in combat zones and after evacuation. The newer types of injuries encountered in this war, such as crush and blast injuries, will be especially considered, together with the prevention and treatment of infections, the treatment of burns and shock and the care of injuries of specific parts of the body. Anesthesia, plastic surgery and the psychoneuroses of war will be some of the other topics. The problems of civilian medical care in wartime will include the following: the responsibilities of individual physicians and hospitals; the personnel problems of hospitals; the organization of emergency medical services; the maintenance of adequate supplies, furnishings and equipment; the preservation of high standards of medical and nursing education and of hospital service in general; hospital public relations; and the necessary administrative adjustments in professional staffs of hospitals. The opening meeting of each session will be devoted to a discussion of the medical and surgical aspects of chemical warfare, led by a representative of the United States Office of Civilian Defense, and the closing meeting will be a panel discussion on problems in wartime civilian medical practice, led by representatives of the United States Public Health Service, the American College of Physicians, the American Medical Association, medical services in industry and the American College of Surgeons. Other topics for consideration at this meeting include endemic and epidemic diseases, medical services in industry, medical and surgical practice, and supplementary postgraduate education for medical officers and civilian physicians.

The schedule for the sessions is as follows:

	CITY	STATES AND PROVINCES	HEADQUARTERS
March 1	St. Paul	Minnesota, North Dakota, South Dakota	Lowsy Hotel
" 3	Milwaukee	Wisconsin, Illinois	Schroeder Hotel
" 5	Indianapolis	Indiana, Kentucky, Ohio	Claypool Hotel
" 8	Detroit	Michigan	Statler Hotel
" 10	Pittsburgh	Pennsylvania, West Virginia	The William Penn
" 12	Buffalo	New York, Ontario	Statler Hotel
" 15	Boston	Massachusetts, Connecticut, Maine, New Hampshire, Rhode Island, Vermont	Statler Hotel
" 17	Brooklyn	New York City, Delaware, New Jersey	St. George Hotel
" 19	Richmond	Virginia, District of Columbia, Maryland	John Marshall Hotel
" 22	Charlotte	North Carolina, South Carolina	Charlotte Hotel
" 24	Birmingham	Alabama, Florida, Georgia	Futwiler Hotel
" 26	Memphis	Tennessee, Arkansas, Mississippi	Peabody Hotel
" 29	Houston	Texas, Louisiana	Rice Hotel
April 1	Kansas City	Kansas, Missouri, Oklahoma	President Hotel
" 3	Omaha	Nebraska, Iowa	Fontenelle Hotel
" 6	Denver	Colorado, New Mexico, Wyoming	Cosmopolitan Hotel
" 9	Salt Lake City	Utah, Idaho	Utah Hotel
" 13	Los Angeles	Southern California, Arizona	Biltmore Hotel
" 16	San Francisco	Northern California, Nevada	Fairmont Hotel
" 20	Seattle	Washington, Montana, Oregon, British Columbia	Olympic Hotel

Dr. Irvin Abell, chairman of the Board of Regents of the American College of Surgeons, in announcing the War

Sessions, said that although participating states and provinces for each meeting have been designated to facilitate arrangements, there will be no geographic restriction on attendance, and those who plan to attend may select the place and time which are most convenient.

The American College of Surgeons canceled its 1942 national meeting and is holding in abeyance plans for a clinical congress in 1943. The regional meeting plan provided by the War Sessions is offered to save the time of physicians and other personnel, and to minimize transportation difficulties, without sacrificing unduly the educational and stimulative benefits of medical assemblies.

CORRESPONDENCE

NEED FOR MEDICAL OFFICERS

To the Editor The need for physicians in the armed forces continues unabated. A large number must be made available from New England in the near future, and since the small communities have done more than their share, many of the future medical officers must come from metropolitan areas.

Physicians of the older age group—forty to fifty—have volunteered freely as have many younger men, yet there is a tendency for some of the latter to wait until called for.

The chief worry on the part of doctors volunteering for the Navy has been a financial one. Yet insufficient attention is paid to the fact that overhead and incidental expenses are immediately cut on entry into service to a degree that largely compensates for the loss of gross cash income received before. Furthermore, the Soldiers and Sailors Relief Act of 1940 protects an officer, his house and his family if he can show that his net income has been substantially reduced.

It is also frequently said that physicians well trained in one field are assigned to duties for which they are ill fitted or which are beneath their professional ability. Although instances of this character do exist, it must be recognized that the exigencies of war may in certain cases render such waste temporarily necessary and, further, and more important, that every effort is made to allocate a man to that position for which he is best fitted. This is the definite, stated policy of the Surgeon General, and it is followed so far as is humanly possible.

The further objection has been raised that often for many months a previously busy physician is comparatively inactive after having been commissioned. Such bore some waiting stems in part from the necessary and vital indoctrination of the Navy and in part from the difficult problem of proper allocation of the individual. Line officers and enlisted men are equally confronted with the same problem.

I urge every physician of military age to volunteer for the Army or the Navy. Whether he is or is not truly essential in civil life can and should be objectively decided by the Procurement and Assignment Service. Those who volunteer will indicate their loyalty to their country and their faith in their fighting comrades.

Applications of interns and residents may be accepted before clearance by the Procurement and Assignment Service if availability is anticipated within twelve months.

If any physician cares to discuss matters concerning his opportunities in the United States Naval Reserve, I shall

be pleased to consult with him any day except Sunday between the hours of 8 00 a m and 3 30 p m

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VERSION EXTRAORDINARY

To the Editor The following quotation is from Herman Melville's *Moby Dick*, a work especially dear to those New Englanders who were born close to salt water. In the annals of obstetrics this case is surely one of the most remarkable.

Queequeg has just delivered Tashtego from the head of the sperm whale. The quotation follows:

Both! both!—It is both!—cried Diggoos again with a joyful shout and soon after, Queequeg was seen boldly striking out with one hand, and with the other clutching the long hair of the Indian. Drawn into the waiting boat, they were quickly brought to the deck, but Tashtego was long in coming to and Queequeg did not look very brisk.

Now, how had this noble rescue been accomplished? Why, diving after the slowly descending head, Queequeg with his keen sword had made side lunges near its bottom, so as to scuttle a large hole there, then dropping his sword, had thrust his long arm far inwards and upwards, and so hauled out our poor Tash by the head. He averred, that upon first thrusting in for him, a leg was presented, but well knowing that that was not as it ought to be, and might occasion great trouble,—he had thrust back the leg, and by a dextrous heave and toss, had wrought a somerset upon the Indian, so that with the next trial, he came forth in the good old way—head foremost.

And thus, through the courage and great skill in obstetrics of Queequeg, the deliverance, or rather delivery of Tashtego was successfully accomplished, in the teeth too of the most untoward and apparently hopeless impediments which is a lesson by no means to be forgotten. Midwives should be taught in the same course with fencing and boxing, riding and rowing.

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NURSES FOR THE ARMED FORCES

To the Editor The careful analysis of the nursing situation by Dr Robert T Monroe, as reported in the January 14 issue of the *Journal*, merits the attention of every physician. The fact of the matter is that we are in a serious predicament and none of the solutions suggested sounds hopeful to me.

We have been altogether too easy in allowing without protest the loss of so many nurses. For after all the greatest amount of illness is not among the armed forces, but right here at home. In fact if the home front is not adequately protected by both doctors and nurses, our output of war materials will be seriously curtailed. With the flight of the practical nurse to more lucrative fields in industrial plants, we cannot afford further weakening of our nursing service despite the demands of the armed

forces. My solution is that enlisted men be trained as nurses by a short intensive course, which will equip them quite as well for nursing as the pharmacist's mate is equipped to take over the medical and surgical care of the men on ships where there are no medical officers. To get this practical and feasible suggestion into actual execution will require considerable effort because of the rigid mental processes of the military. But the civilian has had to change his whole scheme of living, and there is no reason why the military powers-that-be should not cut the pattern according to the cloth. For even though there are ten million men in the armed forces, there are one hundred and twenty million civilians at home.

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BOOK REVIEWS

Surgery of Modern Warfare. By sixty-five contributors. Edited by Hamilton Bailey, F.R.C.S. In two volumes. Vol. II. 4°, cloth, 899 pp., with 325 illustrations. Baltimore: The Williams and Wilkins Company, 1941. \$10.00.

This volume is a continuation of the first one, which has already been reviewed in this column. The general principles of war surgery, with some special sections, were discussed in the first volume. The second volume completes the work on fractures and amputations and considers war surgery of the head, neck and brain.

The material presented has obviously not been written for the specialist in the base hospital, but rather for the officer who starts the patient on his way back from the front. Without a knowledge of what must and can be done in particular cases, it is often difficult for the front-line medical man to make decisions regarding individual cases.

The material included is so varied and extensive that one hesitates to single out any parts for mention. The best of civilian surgery has been taken by a group of experts and adapted to war conditions as their own experience dictates. The chapters on organization of medical service close to the front are fully as important as the rest of the two volumes, for the quality of surgery in war depends greatly on having the man who knows in the right place.

Electrotherapy and Light Therapy, with the Essentials of Hydrotherapy and Mechanotherapy. By Richard Kovacs, M.D. Fourth edition. 8°, cloth, 735 pp., with 314 illustrations and 1 color plate. Philadelphia: Lea and Febiger, 1942. \$8.00.

Seventy-four illustrations were eliminated from the fourth edition of this book on the ground that they were obsolete. For the same reason, similar treatment should have been accorded to the title of the book. "Physical therapy" is a more comprehensive term and one more commonly used for texts of the category to which this treatise belongs. Such a change became even more appropriate when the extra chapters on hydrotherapy, massage and exercises were added, none of which belong to the realm of electrotherapy and light therapy.

The text itself is justly deserving of the popularity that it is apparently enjoying. This is manifested by the fact that within ten years it has run through four editions. Such accomplishment has been made possible by the author's constant vigilance for every form of

progress made in this field. Another factor contributing to the value of this book is the fact that Dr. Kovacs enlisted the aid of several competent men to collaborate with him—each one in his particular field. The result is a comprehensive and an authoritative textbook on physical therapy.

On the whole, good judgment was used in rearranging the material, eliminating some illustrations and diagrams and adding new ones. This is particularly true in the section dealing with short-wave and long-wave diathermy, particularly regarding the underlying theories of electrophysics. The latter is a subject that is confusing and annoying to many an earnest physician who dislikes empiricism. Much more light is needed to clarify short-wave currents—a relatively new physical agent.

Not all changes, however, have been for the better. Thus, the glossary in the preceding editions, which occupied fifteen pages, was a valuable source of information. The reason for its omission from the present edition, which is nine pages shorter than its predecessor, is not evident. Its restoration in future editions will be welcome.

Vaginal Hysterectomy. By James W. Kennedy, M.D., and Archibald D. Campbell, M.D.C.M., F.R.C.S. (Can.), F.R.C.O.G. 4°, cloth, 495 pp., with 44 illustrations. Philadelphia: F. A. Davis Company, 1942. \$10.00.

This book is written by two authors, both of whom use vaginal hysterectomy extensively. The senior author, Dr. Kennedy, is an extremist and enthusiast who is almost on a crusade for vaginal hysterectomy. Dr. Campbell begins his part with a discussion of the anatomy of the female pelvis, and limits his indications to those patients who have a damaged birth canal and need hysterectomy. The authors state that they do not consider vaginal hysterectomy a substitute for abdominal hysterectomy in all cases, but they do emphasize most properly that this procedure has fallen into disrepute in many places simply because a teacher has condemned it through a lack of experience with it. To quote: "We have preceded the general discussion of vaginal hysterectomy by the above admonitions for the reason that we know of no subject in major surgery about which so many ignorant and ignoble statements have been made by teachers as that concerning vaginal hysterectomy."

The indications for this operation that are enumerated by the senior author are without question proper in his hands. However, in the opinion of the reviewer, the use of a surgical procedure must be governed by the ability and training of the surgeon. If one begins to master hysterectomy via the vaginal route by first applying it in prolapse and procidentia, then one may in time so perfect his technic that the operation may be safely used to remove the fibroid uterus. In such matters each surgeon must be the judge of his own limitations and no rules can be stated for his conduct. One can say categorically that various procedures give the same end result in the hands of different operators, for example, the operations for prostatectomy. The lesson of his work is that vaginal hysterectomy should have a place in the repertoire of all those who treat gynecologic patients, and when one becomes expert at it, its indications may be extensive.

There are excellent illustrations of both the clamp and suture methods, and all details of technic are clearly presented. This is a book that should be the library of all who do gynecologic surgery.

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THE RENAL COMPLICATIONS OF LEUKEMIA

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ALTHOUGH many authors¹⁻⁶ have commented on the frequency of leukemic infiltration of the kidneys at some time during the course of the disease, and others^{1, 7-11} have reported the frequency of renal stone and the rare complication of gout,^{1, 10-15} only a few^{7, 8, 16, 17} have suggested taking advantage of these facts in planning x-ray treatment. This is usually of little importance, since all present day methods of treatment in leukemia are merely delaying rearguard actions. However, in an occasional case this knowledge is of benefit to the patient, so that it has seemed worthwhile to call attention once again to these not infrequent complications of a practically invariably fatal disease.

Mach⁶ reported a case of acute myeloid leukemia that at onset showed peripheral edema and urine containing albumin, casts and red and white cells in the sediment, which led to an initial erroneous diagnosis of acute nephritis. There was no azotemia or hypertension. A post-mortem examination showed bilateral leukemic infiltration of the kidneys.

Naegeli¹ has commented on the frequency of "chronic nephritis" in chronic lymphatic leukemia. He has also pointed out the frequency of uric acid stones but the rarity of gout in myeloid leukemia. He, as most other authors on this subject,^{1, 4, 10-15} thinks that the occurrence of gout in leukemia is probably pure coincidence, or that at most the leukemia may be regarded as a contributory factor in a patient with a constitutional predisposition to gout. Bedrna and Polcak⁹ have reported 2 cases of acute ureteral obstruction by uric acid stones complicated by leukemia,—in one myeloid and in the other lymphatic,—in both of which the complication developed shortly following x-ray treatment. In both cases the stones were

removed by ureteral catheterization and the patients were relieved of this acute complication.

Jugenburg and Tschotschia⁷ have reported detailed studies of the uric acid metabolism in patients with leukemia undergoing x-ray treatment. They emphasize the danger of renal failure in these cases, due either to actual leukemic infiltration of renal tissue or to the overloading of kidneys already involved in nonleukemic degenerative lesions, and forced to excrete large amounts of uric acid consequent to the x-ray destruction of high numbers of immature white cells.

One of us (D. M.⁸) has also reported 3 cases of leukemia where renal failure was apparently precipitated by x-ray therapy.

A case of chronic lymphatic leukemia was reported by Cabot¹⁸ in which the patient died seventeen days after the institution of x-ray therapy. The urine showed red and white cells in the sediment, and vomiting began after the first x-ray treatment. The post-mortem examination showed extensive leukemic infiltrations in both kidneys. The course was consistent with death from uremia, but unfortunately no blood-nonprotein-nitrogen or blood-urea studies had been done during life.

In the records of the Pondville Hospital there have been 18 autopsied cases of leukemia during the last nine years. Ten patients had impaired renal function before death. Of these, 4 actually died in uremia (3 of them having nephrolithiasis), 2 others had nephrolithiasis, and 4 had extensive gross and microscopic leukemic infiltration of the kidneys.

The following 3 cases (2 from the Pondville Hospital and 1 from another hospital) are reported in detail in order to emphasize the clinical importance of renal complications in leukemia. Brief abstracts of the 8 other cases from the Pondville Hospital are given at the end of this paper.

CASE REPORTS

CASE 1. H. A. (P.H. 15736), a 61-year-old man, was admitted to the hospital on June 8, 1939, with a diagnosis

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of chronic myeloid leukemia, chronic infectious arthritis and carcinoma of the conjunctiva of the right eye. He had been perfectly well until January, 1937, when one night he suddenly developed burning and itching of the skin of both feet and ankles, lasting about an hour and followed by mild aching in both feet. The next morning both ankles were acutely painful, red, hot, and swollen to about twice their natural size. This initial attack lasted for 2 weeks. From then on there were recurrent attacks of the same type of arthritis, involving first one joint and then another, until it became more or less continuous. The joints most affected were the ankles, knees, right elbow and right wrist. During periods of freedom from pain the patient was able to walk about quite comfortably without crutches or cane. The attacks were never associated with chills, fever or sore throat, and were prone to begin suddenly at night and subside gradually over a period of several days to weeks.

Six months after the first episode of joint pain, the patient had a sudden attack of severe left-sided abdominal cramps, not radiating to the groin or back and not associated with nausea or vomiting. He was admitted to a hospital in another state, where he was discovered to have an enormously enlarged spleen, and after extensive blood and x-ray studies was told that he had an incurable disease for which nothing could be done. However, he felt in his usual excellent health except for the recurrent attacks of joint pain, and so left the hospital against advice. In January, 1939, 6 months before coming to the Pondville Hospital, the patient entered another hospital, where diagnoses of infectious arthritis and myeloid leukemia were made and he was given a course of sixteen x-ray treatments of the spleen without any noticeable effect on the joint pains, which were the only symptoms that bothered him. In May, 1939, the patient was observed to have a white spot on the scleral conjunctiva of the right eye. This grew slowly. A biopsy specimen was diagnosed as epidermoid carcinoma, and he was therefore referred to the Pondville Hospital for x-ray treatment. When admitted he complained only of pain in the joints.

The past history included an episode of profuse bleeding from the gums for 3 days after tooth extractions in 1929, and a similar episode in 1937. Both the parents lived to old age, dying of natural causes. Neither suffered from gout or arthritis.

Physical examination showed a well-developed, fairly well-nourished, plethoric-looking man of 61. Many telangiectases were scattered over the face. There were numerous small tophi in the lobes of both ears, but none were palpable around any of the joints. In the right eye extending over the limbus of the cornea was a small, whitish lesion of the conjunctiva, slightly elevated above the surrounding sclera. The oral mucous membranes were a deep red. There were four remaining badly infected teeth in the lower jaw. The heart and lungs were essentially normal. The blood pressure was 132/85. The spleen was enormously enlarged and extended 3 cm. below the umbilicus and 1.5 cm. to the right of the midline. The liver was also enlarged and extended about 8 cm. below the costal margin. There was a large easily reducible left inguinal hernia, and a smaller one on the right. All the joints appeared to be normal except for the right knee, where there was redness, swelling, heat and fluctuation over the patellar bursa. Both knees were painful on active motion.

Count of white cells and the hemoglobin (Sahli). cc., 31,400,

with 91 per cent polymorphonuclear leukocytes, 2 per cent monocytes, 1 per cent eosinophils, 2 per cent basophils, 2 per cent metamyelocytes and 2 per cent stem cells. The urine was acid, with a specific gravity of 1.020, no albumin and no sugar. The sediment contained innumerable white cells and contained 25 red cells per high-power field. A blood Hinton test was negative. The nonprotein nitrogen was 53 mg., the blood uric acid 8.5 mg., and the creatinine 1.74 mg. per 100 cc. A phenol-sulfonephthalein test showed 25 per cent excretion in the 1st hour and 20 per cent in the 2nd. The basal metabolic rate was +70 per cent. X-ray films of the joints showed no changes characteristic of gout, but microscopic examination of the material obtained from a tophus in the ear lobe showed sodium urate crystals.

Diagnoses of gout, myeloid leukemia and carcinoma of the conjunctiva were made.

The patient remained under practically constant observation from this time until his death on October 31, 1940, approximately 1 year and 5 months later, or 3½ years after the discovery of his splenomegaly.

The conjunctival carcinoma responded to x-ray therapy and was cured in about 1 month's time. The patient's slow downward course was punctuated by increasingly frequent attacks of gout, which responded less and less to colchicine, cinchophen and a diet low in fat and purines. The renal function, which was slightly impaired when he was first studied, diminished steadily. One year after admission phenol-sulfonephthalein excretion had fallen to 5 per cent in 2 hours, though the nonprotein nitrogen still remained around 50 mg. per 100 cc.

Two months before death the white-cell count reached 56,000, and inasmuch as the patient had never reacted well to x-ray therapy, a trial of Fowler's solution was made. In the week following the institution of this treatment the white-cell count dropped to 30,000, but the nonprotein nitrogen rose steadily to 71 mg. per 100 cc. As the patient was clinically on the verge of uremia, the potassium arsenite was stopped and the fluid intake was increased. The nonprotein nitrogen then dropped to 35 mg., but again rose slowly to 63 mg. on the day of death. There was occasional gross hematuria, and almost all the urinary sediments examined had microscopically demonstrable red cells, though there was no clinically recognizable episode of renal colic.

The red-cell count remained between 4,000,000 and 6,000,000 for the first 4 months of observation but then began to fall, and at the time of death was 1,720,000, with a hemoglobin of 20 per cent (Sahli). The white-cell count varied from 12,000 to 60,000, but no differential count showed more than 15 per cent myelocytes.

X-ray treatment was given to the kidneys in the hope of improving the renal function, but no significant benefit could be demonstrated. A course of x-ray treatments was twice given to the spleen, with only slight effect on the white-cell count, and each time with a severe exacerbation of the gout. However, since the patient had had so many attacks of gout and the x-ray treatments were spread out over a week's time, it is impossible to be sure that the latter increased the gout. At all events, the patient was not helped by the x-ray treatment. The trial of Fowler's solution, as mentioned above, resulted in a rapid temporary drop of the white-cell count but coincided with an alarming rise of the nonprotein nitrogen, so that this too was discontinued. The patient finally died with extreme cachexia, profound anemia and chronic renal insufficiency.

Autopsy The spleen weighed 1360 gm, and the liver 2475 gm. The kidneys were of normal size, weighing 110 gm each. There was a large stone in the pelvis of the right kidney, and several small ones in the calyces on the right. There was also a small stone in the lower end of the right ureter just proximal to the opening into the bladder. Microscopic examination of the kidneys showed relatively normal findings except for the presence of masses of leukocytes and myelocytes in the blood vessels and a small area of leukemic infiltration in the cortex. The bone marrow showed the characteristic picture of chronic myeloid leukemia.

In brief, this patient had chronic myeloid leukemia and gout. During his last 4 years of life practically all his symptoms were due to gout, although renal insufficiency was a factor in the last year and a half. An incidental finding was a carcinoma of the conjunctiva of the right eye that was cured by radiation therapy. At autopsy the diagnosis of leukemia was confirmed and multiple renal calculi (pelvic and ureteral) were found that doubtless were a contributory if not the main cause of his impaired renal function. The similarity of this case to the one reported by Reifstein¹⁴ is striking.

CASE 2 E M H (P H 19588), a 28-year-old, married woman, was admitted to the hospital on November 9, 1941, for x-ray treatment on the basis of a previous diagnosis of lymphosarcoma. She had been perfectly well until 4 months previously, when she began to have marked frequency of urination during the day and had to void twice during the night. This continued for 2 months but was not associated with any other symptoms. She felt perfectly well and the frequency gradually disappeared. Six weeks prior to entry she began to have moderately severe lower abdominal pain, chiefly on the left but sometimes in the right groin. The pain came on gradually and lasted for several hours, and was apt to be worse at night. It was sometimes knife-like and severe enough to double her up, but at other times it was merely a dull ache. There was some loss of appetite, and mild indigestion. Occasionally the patient was feverish and once or twice had profuse night sweats. At about the time the abdominal pain began she first noticed some painless swellings in her neck, and subsequently more and more lumps appeared in both sides of the neck and behind the ears. She had also noticed a tendency to bruise more easily than usual in the preceding few weeks, and had been menstruating for 10 days at the time of admission. There had been gradually increasing dyspnea for the preceding 2 months. She had been seen in another hospital, where a lymph node had been removed from the neck for diagnostic purposes. A diagnosis of lymphosarcoma had been made on the section so that she was referred to the Pondville Hospital for x-ray therapy.

The past history included osteomyelitis of the left leg at 7 and removal of the appendix and an ovarian cyst at 24.

Physical examination showed a well-developed, pale, obese woman with masses of discrete firm nodes in both sides of the neck. Enlarged nodes could also be felt in front of and behind both ears, in both axillas and in both groins. The nodes were firm and discrete and varied

in diameter from 0.5 to 2.0 cm. There were purpuric spots on the skin of the chest and left arm. The gums and mucous membranes were pale but showed no hemorrhages. The heart and lungs were within normal limits. The blood pressure was 160/85. The abdomen was distended tympanically, and tender in both lower quadrants. The spleen was felt two fingerbreadths below the costal margin. The legs were obese but there was no pitting edema.

The red-cell count was 1,700,000 and the hemoglobin 30 per cent (Sahli). The white cell count was 4000, with 40 per cent polymorphonuclear leukocytes, 21 per cent lymphocytes, 1 per cent basophils, 4 per cent metamyelocytes and 32 per cent extremely large immature cells, thought to be lymphoblasts. The red cells showed marked variation in size and shape, and occasional nucleated red cells were seen. A blood Hinton test was negative. The urine showed a specific gravity of 1.015, the slightest possible trace of albumin and no sugar. The sediment contained occasional red cells and 8 white cells per high power field, with occasional clumps of the latter. The blood nonprotein nitrogen was 20 mg per 100 cc.

A diagnosis of acute lymphatic leukemia was made. The prognosis was considered extremely grave, but the patient was given repeated transfusions (3500 cc of blood in seven transfusions), and as she continued to bleed from the uterus was given radiation therapy to the pelvis in the hope of stopping the bleeding.

On November 27, 18 days after admission a generalized convulsion occurred and the blood pressure was 240/130. The urine showed a large trace of albumin and many red and white cells in the sediment. The blood nonprotein nitrogen was 66 mg per 100 cc. The patient was drowsy, there was pitting edema of the legs and face, and the eyes were puffy. The nonprotein nitrogen continued to rise, reaching 80 mg on December 1. Because of the possibility that these manifestations of acute nephritis were due to leukemic renal infiltration, a course of x-ray treatments was given to the kidneys. This was followed by improvement, with a gradual drop of the nonprotein nitrogen to 30 mg on December 13. The facial edema gradually cleared, but the edema of the legs remained about the same. The blood pressure had dropped to 170/120 by November 30 and was 180/105 on December 7, when another series of x-ray treatments was begun to the region of the kidneys. There was a slight further drop to 170/110 on December 4 and to 170/90 on December 15, and finally to 110/65 on December 16, the day of death. Thoracostomies were done on December 6 and 13, with the removal of 1800 cc of clear, yellow fluid each time. In spite of the apparent improvement of kidney function the patient failed rapidly and died about 5 weeks after admission. During these weeks the hemoglobin had varied from 30 to 53 per cent (Sahli) and the white cell count from 4000 to 2000. The large, immature white cells varied from 2 to 36 per cent.

Autopsy There were bilateral pleural effusions, enlargement of the spleen (weight 350 gm) and of the liver (weight 1900 gm) and a large retroperitoneal tumor. Around the aorta, in both the thoracic and abdominal portions, there were many enlarged lymph nodes, and in addition there was a diffuse infiltration of the adjacent areolar tissue by yellowish, firm tissue similar in appearance to that of the lymph nodes. This tissue was quite dense and was hard to dissect from the vertebral bodies. Retroperitoneally, particularly in the lower left portion this para-aortic tumor was extensive, completely surround-

ing the great vessels, the renal vessels, both ureters, the adrenal glands and the pancreas, and infiltrating and practically surrounding the pelvic organs. The tumor also extended along the femoral vessels into both legs. The tracheobronchial and mesenteric lymph nodes showed only slight enlargement. No ante-mortem thrombi were found in any of the compressed blood vessels. The kidneys were somewhat enlarged, the right kidney weighing 250 gm. and the left 180 gm., and there were multiple small urate stones in the right kidney, pelvis and calyces. On microscopic examination the kidney sections showed extraordinarily few abnormalities. A section from the left kidney showed slight interstitial fibrosis and tubular dilatation, which were not present on the right. Sections from both kidneys showed normal glomeruli, but in the convoluted tubules there were epithelial swelling and granularity and some nuclear pyknosis. Many tubules contained amorphous material, and a few contained granular casts. The peripelvic tissues showed neoplastic cellular infiltration, but the kidney parenchyma did not. Histologic examination of the tumor masses showed a neoplasm that was diagnosed as Hodgkin's sarcoma by Dr. Frederic Parker, Jr., of the Mallory Institute of Pathology. In addition, the spleen and bone marrow showed an infiltration of cells without the formation of tumor nodules.

In retrospect one cannot be certain of the cause of this patient's episode which simulated acute nephritis. She did have multiple renal calculi on the right, and both ureters and renal arteries and veins were imbedded in tumor tissue. The kidneys themselves showed practically no infiltration with tumor, though they had received x-ray treatments, followed by a temporary improvement of renal function. The most likely explanation seems to be impairment of renal function through mechanical obstruction of the ureters and renal blood vessels by extrarenal tumor, but renal calculi on the right may also have been a contributory factor. In summary, this patient with acute leukemia had an episode simulating acute nephritis with edema, hypertension, convulsions and nitrogen retention, which subsided following x-ray therapy to the kidneys. At autopsy she was found to have multiple renal calculi, and both ureters and renal arteries and veins were imbedded in tumor tissue that was diagnosed as Hodgkin's sarcoma.

CASE 3. S. C. (C.H. 9068),* a 68-year-old woman, came under medical observation in October, 1941, because of increasing dyspnea, fatigability, weakness and weight loss of 1 year's duration. She was found to have signs suggestive of early cardiac decompensation and was put to bed and digitalized. She soon became nauseated, so that the digitalis was stopped. Two weeks after being put to bed she developed phlebitis, which gradually spread in the next 5 weeks to involve both legs from groin to ankle. Her appetite was poor; she felt weak, became increasingly pale and ran a daily temperature of about 100°F. A specimen of urine showed a large amount of albumin, but in a second one examined several weeks later

the albumin was within normal limits. The patient had no cough or dyspnea while lying in bed, but because of her rapid downhill course with increasing pallor and weakness she was sent to the Cambridge Hospital.

On admission, 7 weeks after her first visit to a physician, the patient presented a picture of marked pallor and debility. The heart was enlarged, the apex impulse being in the anterior axillary line. There were occasional premature beats, and a systolic murmur was heard all over the precordium. The heart rate was 100, and the blood pressure 130/40. The lungs showed dullness at the left base, with bronchial breath sounds and coarse rales. The liver was felt one fingerbreadth below the costal margin, and the tip of the spleen was felt 1 cm. below the left costal margin. There was gross edema of the left leg from the groin to the toes, with induration and tenderness in the popliteal space. The right leg was slightly swollen above the knee and considerably swollen below it.

The red-cell count was 2,560,000 and the hemoglobin 42 per cent (Sahli). The white-cell count was 409,600, with 32 per cent polymorphonuclear leukocytes, 14 per cent band forms, 2 per cent lymphocytes, 34 per cent myelocytes, 12 per cent metamyelocytes, 4 per cent basophils and 3 per cent myeloblasts. The urine was yellow and cloudy, with a specific gravity of 1.006, a very slight trace of albumin and no sugar. The sediment contained from 10 to 20 white cells per high-power field and numerous hyaline casts. The blood nonprotein nitrogen was 250 mg. per 100 cc. A blood Hinton test was negative. X-ray examination of the chest showed a small amount of fluid and some pneumonia at the left base. A second white-cell count the day after admission was 590,000. The patient had increasing dyspnea for 3 days and died suddenly on the 4th day.

Autopsy. In addition to the usual findings in myeloid leukemia, there was thrombosis of both femoral and iliac veins, as well as multiple small pulmonary emboli. There was a small patch of bronchopneumonia. The heart weighed 290 gm., and showed mild arteriosclerosis and arteriolar sclerosis and a small mural thrombus in the apex of the right ventricle. The kidneys were of considerable interest in view of the high nonprotein nitrogen (250 mg. per 100 cc.) 3 days before death. They weighed 160 gm. each and were grossly normal. There were no stones in the pelvis or ureters. Microscopic examination, however, showed considerable arteriosclerosis of the renal arteries and arterioles, and almost complete stasis throughout the vascular channels, beginning in the glomeruli, continuing in the intertubular capillary system and being most obvious in the large, dilated veins. Most of the glomeruli were intact, and the capsules were not thickened. Many showed dilatation of the afferent arterioles and of the glomerular-tuft capillaries, which were distended with blood cells, mostly primitive white cells, some of which were undergoing mitosis. There were foci of leukemic cells within the interstitial tissue, especially around the large veins, but they apparently played little or no role in mechanical obstruction of the tubules. It was thought that the uremia could be explained on the basis of a failing circulation with stasis and obstruction of the glomerular capillaries.

In brief, this elderly woman with leukemia, thrombophlebitis of both iliac and femoral veins and multiple small pulmonary infarcts died in uremia. Her renal insufficiency was due in part to circula-

*Reported through the courtesy of Dr. Gordon A. Saunders, of Arlington.

tory failure and anemia and in part to blocking of the glomerular capillaries with leukemic cells

SUMMARY

Attention is once again called to the frequency of renal failure in leukemia. The causes of this complication are nephrolithiasis, infiltrative leukemic lesions of the kidneys, obstruction of renal blood vessels or ureters by leukemic tissue, or finally nonleukemic degenerative lesions of the kidneys. The rare occurrence of gout in cases of leukemia is noted. Three cases exemplifying these complications are reported.

It is hoped that knowledge of these complications may occasionally be of help in planning the treatment of this incurable disease.

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BRIEF ABSTRACTS OF THE OTHER CASES AT THE PONDVILLE HOSPITAL

CASE 4 E M S (PH 11306, previously reported in detail⁸), a 65 year old woman, who had had a mass in the left upper quadrant of the abdomen for several years, a mass in the left breast for 8 years, and had recently lost 75 pounds, was found to have a small hard, nodular, ulcerated mass in the left breast, a palpable hard lymph node in the left axilla and an enormously enlarged spleen. The blood picture was characteristic of chronic myeloid leukemia, with a white-cell count of 380,000 and a blood nonprotein nitrogen of 65 mg per 100 cc. The urine showed a specific gravity of 1.016 and a trace of albumin, with red and white cells in the sediment.

Following x-ray therapy the white-cell count dropped to 25,100, but the patient died in uremia with a nonprotein nitrogen of 188 mg per 100 cc.

Autopsy showed chronic myeloid leukemia and carcinoma of the left breast with axillary metastases. The kidneys showed some grayish white, inspissated material in the right pelvis and microscopically there were foci of lymphocytic infiltration hyalinized glomeruli atrophied tubules and subintimal thickening in the large blood vessels. In the pelvic fat in one section there was a mass of loose connective tissue in which were collections of leukemic cells.

CASE 5 W C (PH 12612), a 71 year old man was admitted because of loss of appetite a weight loss of 75 pounds and diarrhea of 3 months duration. There had been an eruption on the back of both hands for 6 weeks. On examination he was found to have skin lesions on the backs of both hands and of the right forearm consistent with pellagra. There were large masses of soft lymph nodes in both axillae and inguinal regions and an enormously enlarged spleen. The blood showed the characteristic picture of chronic lymphatic leukemia. The white cell count was 199,000 with 97 per cent lymphocytes and the red cell count was 1,730,000 with a hemoglobin of 37 per cent (Sahli). The nonprotein nitrogen was 31 mg per 100 cc and the urine sediment showed red and white cells and occasional hyaline casts.

X-ray treatment was given to the spleen with a drop in the white cell count to 112,600 but without much clinical benefit. Six months later because of increasing dyspnea and weakness the patient was readmitted and died 8 days later. Shortly before death the white cell count was 167,000, with 95 per cent small lymphocytes, and the red cell count was 1,400,000, with a hemoglobin of 75 mg (Sahli).

Autopsy revealed the usual findings of chronic lymphatic leukemia. The kidneys showed gross and microscopic scattered areas of tumor infiltration.

CASE 6 A McD (PH 12941, previously reported in detail⁹), a 56 year old man was admitted with a history of increasing weakness, pallor and a weight loss of 30 pounds in 3 years. He was found to have an enormously enlarged spleen and the blood findings were those of chronic myeloid leukemia, with a white cell count of 237,500, a red cell count of 2,940,000 and a hemoglobin of 54 per cent (Sahli). A phenolsulfonphthalein test showed 15 per cent excretion in the 1st hour and 15 per cent in the 2nd.

X-ray treatments were given to the spleen from time to time during the next 21 months, with considerable benefit. On the 4th hospital admission the spleen was enormously enlarged, the white cell count was 210,000, and the hemoglobin was 60 per cent. The blood nonprotein was 47 mg per 100 cc. Following x-ray treatment the white-cell count fell steadily to 3800 in 1 month. The blood nonprotein nitrogen, however, rose steadily to 244 mg and the patient died in uremia.

Autopsy showed the usual findings of chronic myeloid leukemia. The kidneys were of particular interest. Both contained multiple uric acid and urate calculi in the calyces, and the upper portion of the ureter was packed with gravel. Sections from the right kidney showed evidence of an active pyelonephritis.

CASE 7 H S E (PH 15613), a 54 year old man, was admitted because of enlarged painless lymph nodes of 1 year's duration. He was found to have tremendously enlarged cervical supraclavicular axillary and inguinal nodes. The liver and spleen were not felt. X-ray films

showed enlarged mediastinal nodes. The white-cell count was 3000, with 50 per cent polymorphonuclear leukocytes, 49 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils, but with a later lymphocyte percentage of 80 when the total cell count was 3400. The red-cell count was 3,110,000, with a hemoglobin of 52 per cent (Sahli). The nonprotein nitrogen was 52 mg., and the blood uric acid 8 mg. per 100 cc. A phenolsulfonephthalein test showed 45 per cent excretion in 2 hours, and the basal metabolic rate was +80 per cent. The urine showed a slight trace of albumin, and the sediment contained a few finely granular and coarsely granular casts and 10 white cells per high-power field.

X-ray therapy was given to both kidneys and to the right side of the neck. The nonprotein nitrogen dropped to 39 mg. and the blood uric acid to 4 mg. per 100 cc. The white-cell count dropped to 1800, with 60 per cent lymphocytes. The patient continued to feel well, but because of his leukopenia he was transfused. The next day he developed pulmonary edema and died.

Autopsy showed the changes of chronic lymphatic leukemia and of septicemia. The kidneys contained numerous small foci of lymphocytes scattered irregularly throughout, although slightly commoner in the cortex. There were no stones.

CASE 8. F. S. (P.H. 16077), a 37-year-old man, was admitted because of multiple hemorrhagic tumors of the skin of 9 weeks' duration. He had lost between 15 and 20 pounds in weight and had rapidly become worse in spite of x-ray treatment. The entire body had a purplish-red hue. Scattered over the neck, chest and all four extremities were numerous purplish-red, hemorrhagic, soft tumor nodules, imbedded in the skin and freely movable over the underlying structures. These varied in diameter from 1 to 8 cm. There were firm, enlarged lymph nodes in the neck, axillas and groins, which were matted together. There was marked edema of both legs, the abdominal wall, penis and scrotum. Almost the entire skin of the body appeared to be infiltrated with tumor and had a thick, leathery feeling. Many places were ulcerated and weeping. There was a marked gingivitis involving both upper and lower gums, which appeared hyperplastic and hemorrhagic. There were many large and small submucosal hemorrhages. The spleen and liver could not be felt. The white-cell count was 10,400, with 66 per cent polymorphonuclear leukocytes, 29 per cent lymphocytes, 4 per cent monocytes, 1 per cent myelocytes and 2 per cent nucleated red cells. The red-cell count was 2,250,000, with a hemoglobin of 35 per cent (Sahli). Three days later the white-cell count was 5900, with 79 per cent polymorphonuclear leukocytes, 20 per cent lymphocytes, 1 per cent myelocytes and 7 per cent nucleated red cells. The nonprotein nitrogen was 53 mg. per 100 cc. on entry but rose to 111 mg. 2 days later. The urine showed only the slightest possible trace of albumin, and the sediment contained 17 red cells and 1 white cell per high-power field. The patient went rapidly downhill and died 5 days after admission.

Autopsy showed extensive infiltration of practically every organ of the body with lymphoblasts. The kidneys showed heavy subcapsular, periglomerular and perivascular tumor-cell infiltration involving a large proportion of the cortical areas but almost absent in the medullas.

CASE 9. M. J. (P.H. 16198), a 71-year-old man, was admitted because of generalized lymphadenopathy, hepatomegaly and splenomegaly of 1 month's duration. He was semicomatose on admission and died 5 days later. On admission the nonprotein nitrogen was 102 mg. per cc. and the urine essentially normal. The white-cell count was 18,300, with 78 per cent polymorphonuclear leukocytes, 3 per cent lymphocytes, 5 per cent monocytes, 8 per cent metamyelocytes, 2 per cent hemohistioblasts and 4 per cent hemocytoblasts. The red-cell count was 4,180,000 with a hemoglobin of 83 per cent (Sahli).

Autopsy showed an acute stem-cell leukemia. The kidneys showed minute foci of as well as diffuse infiltration with tumor cells, most marked in the cortices.

CASE 10. E. G. (P.H. 16952), a 76-year-old woman, was admitted because of vaginal bleeding for 2 weeks. She was found to have an extensive carcinoma of the cervix. Blood studies, however, also showed the presence of acute myeloid leukemia. The white-cell count was 99,700 with 1 per cent polymorphonuclear leukocytes, 1 per cent lymphocytes, 2 per cent myelocytes, 1 per cent promyelocytes, 87 per cent myeloblasts and 8 per cent hemocytoblasts. The red-cell count was 2,500,000, with a hemoglobin of 50 per cent (Sahli). The blood nonprotein nitrogen was 32 mg. per 100 cc. The urine showed a moderate amount of albumin, and the sediment contained 15 red cells and 50 white cells per high-power field. In spite of x-ray treatment the patient died 23 days after admission.

Autopsy showed advanced carcinoma of the cervix with extension to the vaginal wall and broad ligaments, metastatic involvement of the right parailiac and para-aortic lymph nodes and metastases to the lungs. There were also the characteristic changes of acute myeloid leukemia. The kidneys showed a generalized intracapsular and perivascular infiltration with leukemic cells, as well as a patchy infiltration of the interstitial tissues, most marked in the cortices and in the peripelvic fat.

CASE 11. J. H. G. (P.H. 17640), a 75-year-old man, was admitted because of vomiting of 12 weeks' duration. He had received x-ray therapy at another hospital because of a blood picture of lymphatic leukemia. There were scattered petechiae under the tongue and in the skin over the chest. The spleen and liver were both considerably enlarged. There were no significantly enlarged peripheral lymph nodes. The white-cell count was 9400, with 26 per cent polymorphonuclear leukocytes, 6 per cent lymphocytes and 68 per cent lymphoblasts. The red-cell count was 9400, with a hemoglobin of 25 per cent (Sahli). The blood nonprotein nitrogen was 61 mg., and the blood uric acid 7.1 mg. per 100 cc. The urine contained a very slight trace of albumin, with 5 red cells per high-power field in the sediment. The patient became rapidly weaker, had bloody and tarry stools and developed additional cutaneous hemorrhages. He died 23 days after admission.

Autopsy showed the characteristic findings of lymphatic leukemia. In the left kidney there were several small calculi in the calyces, and there was a large stone in the upper portion of the left ureter. Microscopic examination showed several small scars of old infarcts and a few foci of tumor cells, but the latter were most numerous in the peripelvic fat.

RENAL HYPERTENSION

A Review of Its Status, Including the Report of a Case of
Hypertension Relieved after NephrectomyLIEUT BENJAMIN V. WHITE (MC), USNR,* RALPH E. DURKEE, MD,[†] AND
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SINCE Goldblatt's¹ publication in 1934, there has been widespread interest in the relation of the kidneys to hypertension. This has been manifested by reports of occasional crises of hypertension associated with unilateral renal disease in which the blood pressure was lowered following the removal of the offending kidney. The number of such reports has not been great, but some of the cases are so clear that there is no doubt of their validity.²⁻¹⁵ There have also appeared several surveys of large numbers of hypertensive patients in which attempts have been made to classify the etiology of the disease. Although these reports have shown the presence of many types of renal disease in some cases of hypertension, and a higher incidence of hypertension in patients with renal disease than in those without, more precise correlations have been generally disappointing.¹⁶⁻²¹ It is the purpose of this communication to review certain data with a bearing on this subject.

EXPERIMENTAL PHYSIOLOGY

Although Tigerstedt and Bergman² in 1896 isolated a vasopressor substance of renal origin, which they named "renin," and Janeway²³ subsequently succeeded in producing occasional hypertensive dogs by renal surgery, Cash²⁴ in 1924 was the first able to produce experimental hypertension consistently. His technic included excision of renal tissue and ligation of the renal vessels. His experiments were numerous, were carefully correlated, and included tests of renal function. His conclusions were consistent with subsequent experimental surgery and study of renal extracts. The Cash preparation is symbolized in Figure 1C. Cash concluded, first, that reduction of renal tissue by excision and by ligation of the renal vessels was followed under certain circumstances and in most cases by a rise of both systolic and diastolic blood pressures and in all cases by a rise in diastolic pressure averaging 27 mm; that the required conditions were that 50 per cent of the kidney substance be removed and that the portion deprived of its circulation remain in situ; that necrosis alone

or excision of one kidney alone produced no change in blood pressure; that after hypertension reached its peak in four or five days it tended to return to normal, the rate of return being proportional to the amount of good tissue left; and that after removing 25 to 85 per cent of the renal tissue no retention of nonprotein nitrogen occurred, whereas dye excretion was impaired after 50 per cent of the kidney tissue had been removed.

Although Cash's monumental work established the framework for the subsequent understanding of the action of renal extracts, it was Goldblatt¹ who precipitated a wide interest in that study. He found that sudden clamping of both renal arteries produced marked hypertension with uremia, a condition that he compared to malignant hypertension in man (Fig 1E). Less severe bilateral clamping produced sustained elevation of blood pressure with prolonged life but no nitrogen retention and only occasional impairment of the urea clearance (Fig 1D). Gradually increased clamping, however, produced very little change in blood pressure, a finding that Goldblatt attributed to the development of collateral capsular circulation. He also showed that experimental renal hypertension is independent of the adrenal glands or of the blood concentration of guanidine, and Page²⁵ subsequently showed that it is independent of the afferent nerves of the kidney.

Other surgical methods of producing hypertension also exist. Page,^{25, 26} in attempting to find a method of preventing collateral capsular circulation, wrapped dogs' kidneys in cellophane (Fig. 1G). The animals became hypertensive. The cellophane broke down into a fibrocollagenous hull that stimulated proliferation and led to perinephritis. Harrison, Mason, Resnick and Rainey²⁷ found that bilateral clamping of the ureters generally produced hypertension with uremia (Fig. 1F), whereas bilateral nephrectomy resulted in uremia without hypertension (Fig. 1B).

The fact that certain methods (Fig. 1F and G) did not involve occlusion of blood vessels led Corcoran and Page^{28, 29} to a study of blood flow through kidneys of animals rendered hypertensive by the Goldblatt technic. If pulse pressure was reduced by partial occlusion of the renal arteries

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and the arterial blood pressure was experimentally increased to permit the normal volume of blood flow, hypertension still occurred. This work sug-

removal of the sound kidney resulted in increased hypertension, whereas removal of the cellophane kidney resulted in the return of the blood pressure to normal. These observations were also true of a unilateral Goldblatt kidney.³⁰

The experimental surgical procedures illustrated in Figure 1 have been interpreted as indicating that a pressor substance is mobilized in ischemic (or otherwise damaged) renal tissue. The fact that this substance can best be demonstrated after removing large amounts of normal kidney has led many investigators to the belief that normal kidney tissue elaborates a substance that inhibits this pressor reaction.*

RENAL EXTRACTS

Because of the existence of many pressor substances of nonspecific nature and the absence of any experimental evidence of their clinical importance, Tigerstedt and Bergman's isolation of renin attracted little attention until Goldblatt's¹ work, confirming Cash's earlier observations,²⁴ became widely publicized.

In 1938, Merrill, Williams and Harrison³¹ reported studies in which they established certain differences between Tigerstedt and Bergman's renin and nonspecific vasopressor substances. Page³² also studied the physiologic action of renin. He found that when it was administered to an animal over a period of time its pressor action tended to disappear, an exhaustion phenomenon that he termed "tachyphylaxis."

In 1939, Page and Helmer³³ found that renin produced no vasoconstriction when perfused with Ringer's solution through a rabbit's ear, but that vasoconstriction did occur if a proteinlike substance, called "renin-activator," derived from red blood cells or plasma, was added. Subsequently, they found that renin and renin-activator could be incubated together to yield a third substance that would produce a sharp adrenalinelike effect. To this substance they gave the name "angiotonin." They described it as a fluorescent substance whose degree of fluorescence was proportional to its pressor activity. They stated that it was heat-stable in acid solutions, and that crystalline oxalates and picrates had been formed from it. Following the work of Muñoz, Braun-Menendez, Fasciolo and Leloir,³⁴ Page and Helmer³³ suggested that renin was an enzyme, that renin-activator was a substrate, and that the end product of their reaction was angiotonin (Fig. 2).

There is evidence that in addition to pressor substances, certain inhibitors also exist. Freeman³⁵ showed that if blood was transfused from normal

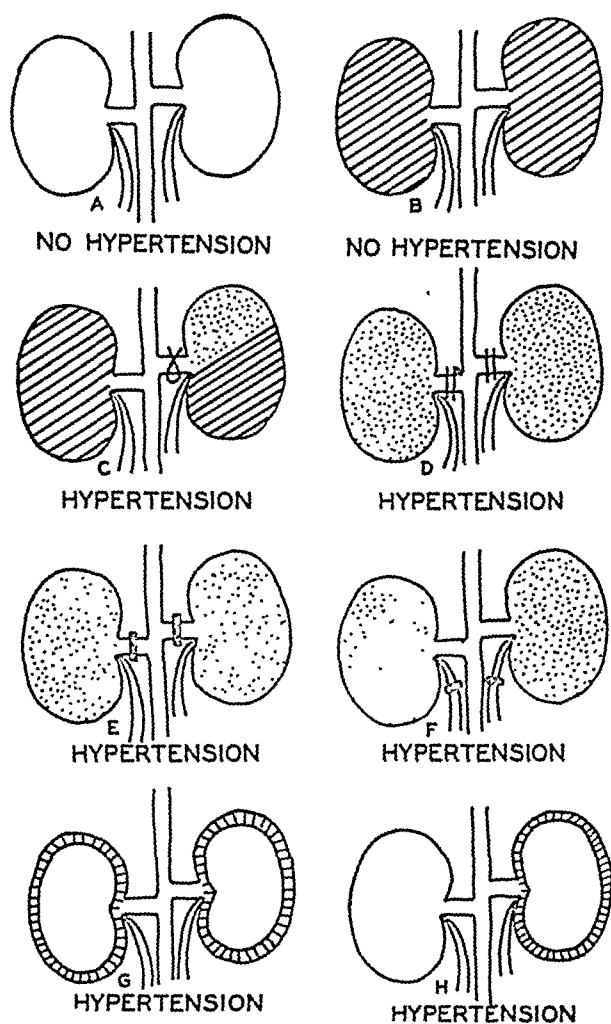


FIGURE 1. *Experimental Hypertension in Animals.*

A—normal kidneys; B—bilateral nephrectomy (usually accompanied by uremia but not by hypertension); C—ligation of renal vessels, with extirpation of nonischemic renal tissue; D—moderate sudden clamping of renal arteries; E—severe sudden clamping of renal arteries; F—obstruction of both ureters; G—cellophane perinephritis.

Hypertension occurs in all these preparations except A and B. In E and F the hypertension is associated with uremia. Preparation H represents a unilateral cellophane kidney. In this, there occurs only a moderate degree of hypertension, which is accentuated if the normal kidney is removed, and disappears if the cellophane kidney is removed. Note that in all instances the injured renal tissue remains in situ. Preparations C and H illustrate the protective influence of normal kidney substance.

gested that some factor other than ischemia per se was responsible for hypertension.

Where hypertension resulted from a unilateral cellophane kidney (Fig. 1H), Page showed that

*An alternative explanation for the protective influence of normal renal tissue is that it excretes the pressor substance. This view is apparently held by most members of the South American group.

dogs to dogs rendered hypertensive by the Goldblatt technic, a fall in blood pressure lasting from six to thirty-one minutes would occur. This sustained fall did not occur when hypertensive dogs were transfused with hypertensive dogs' blood or when normal dogs were transfused with normal dogs' blood.

Page and Helmer³⁶ considered that tachyphylaxis, or the diminishing effect of renin administered intravenously, was explained by two mecha-

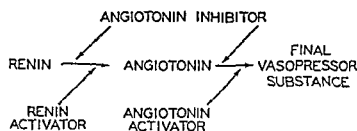


FIGURE 2 The North American Concept of the Vasopressor Mechanism

Renin is a substance mobilized by injured renal tissue. It reacts with renin activator (a normal constituent of plasma) to produce angiotensin, which has a sharp, adrenalin like effect. Page has produced evidence that the angiotensin then reacts with another constituent of plasma, angiotensin activator, to yield a final vasopressor substance. Inhibitors are not clearly differentiated into those that act on renin and on angiotensin respectively.

South American workers, using different terminology, substantiate the formation of a stable vasopressor substance (presumably angiotensin) from renin and a constituent of plasma. Their evidence suggests that it is the final vasopressor substance. The South American group has found an enzyme that breaks down their substance, but no specific inhibitors.

nisms—first, the exhaustion of the supply of renin activator and, second, the presence of so-called "renin-inhibitor." Tachyphylaxis was found to occur to a lesser extent with angiotensin, and angiotensin activator was found to be present in an acetone soluble fraction of blood. These workers therefore concluded that angiotensin was probably an intermediary substance and not the final pressor agent. They were unable to differentiate the inhibitory substances in their actions on renin and angiotensin, respectively (Fig. 2). It is generally believed that renin is a substance abnormally liberated as the result of renal injury and that renin activator and angiotensin activator are normal constituents of blood.

Work similar to that of Page and his co-workers was carried out independently in Buenos Aires. Muñoz, Braun-Menendez, Fasciolo and Leloir^{34, 37, 38} showed that renin had the properties of an enzyme and that the blood globulin factor was a substrate. By incubation *in vitro* they found that these two substances formed a third

substance with the same physiologic characteristics as a vasoconstrictor substance isolated from the venous blood of ischemic kidneys. This third substance, probably identical with angiotensin, they called "hypertensin." The South American group also found that the enzymatic formation of hypertensin was limited by another enzyme that they called "hypertensinase." This substance was found to be present in extracts of many body tissues, especially plasma, liver and spleen.

Hypertensin was shown by these workers, and also by Dexter,^{39, 40} to produce no tachyphylaxis when injected into intact animals—although it did so in the isolated rabbit's ear. It is probable, therefore, that the hypothesis of an angiotensin-activator and a final vasopressor substance may eventually be discarded.

INHIBITORY SUBSTANCES

Regarding the nature of possible inhibitory substances there is a wide divergence of opinion. Page⁴¹ found that bilateral nephrectomy increased the pressor response to renin and angiotensin and greatly increased the amounts of these substances needed to produce tachyphylaxis. He concluded, therefore, that in nephrectomized animals the inhibitory substances are not present, and conversely that inhibitors are present in the kidneys of normal animals. Harrison⁴² also found that certain pressor substances were more effective in nephrectomized than in normal animals, and concluded that inhibitors exist in normal kidney tissue. The presence of such inhibitors was also suggested by the rise in blood pressure that followed the removal of the normal mate to an ischemic kidney. Conclusions based on increased vasoconstriction in uremic animals must be recognized as open to doubt because of the great vascular sensitivity of such preparations and the confused biochemical balance produced by the retention of metabolites. There is evidence, however, that certain substances capable of neutralizing the action of renin or angiotensin in animals do exist. This problem is now being attacked on the basis of three different concepts, as follows:

(1) The members of the Buenos Aires group are unconvinced of the existence of any specific inhibitor of renal origin. They have produced evidence for the existence of an enzyme, widely disseminated through body tissues, which is capable of destroying the circulating vasopressor substance (hypertensin). Recently Schroeder, Stock and Dobriner,⁴³ in this country, have demonstrated the effectiveness of aminoxidase isolated from liver tissue in inhibiting the action of a vasopressor substance (presumably angiotensin) in rats. It is probable that hypertensin and an-

giotonin are identical. It is possible that aminoxidase, or some related substance, is the hypertensinase of the South American workers.

(2) Wakerlin and Johnson⁴⁴ have demonstrated in dogs the formation of an antibody to pig's renin. They injected this substance into hypertensive Goldblatt dogs and obtained a definite fall in blood pressure, whereas the substance has been found not to lower the blood pressure of normal animals. It is unfortunate that the titer of antibody has in some cases been shown not to parallel the blood-pressure response.⁴⁰

(3) Other American workers have been engaged in the study of specific inhibitors of renal origin. Page and his associates⁴⁵ isolated a substance with which they treated a large number of patients. Although definite reduction in blood pressure usually resulted, the greatest effect was noticed when a febrile or local tissue reaction occurred. The possibility of a nonspecific foreign-protein effect cannot be entirely dismissed. Grollman, Williams and Harrison⁴⁶⁻⁴⁸ have also been working in this field and have demonstrated the blood-pressure-lowering effect of extracts of renal substance on hypertension in rats, dogs and human beings. They have recently further fractionated their extract⁴⁹ so as to eliminate the nonspecific action of concentrated salt, an error to which their earlier experiments were possibly subject. Although the new extract has been used only in rats, it appears to be specific in its effect. It requires 200 to 300 gm. of kidney to prepare one day's dose for a rat.

RENAL HYPERTENSION IN MAN

Although the renin mechanism in animals has been firmly established, direct evidence of its existence in man depends on perfusion experiments through isolated organs, a technic that is open to many nonspecific results. Many of the clinical reports of cases of human hypertension cured by nephrectomy are not entirely convincing. The following case history is unique in that the patient was followed for two years with normal blood pressure before the development of his illness and for one full year after nephrectomy.

CASE REPORT

A 39-year-old, married automobile service agent was first seen by one of us (R. E. D.) on September 17, 1933, because of recurrent episodes of low-back pain and vague abdominal discomfort, characterized chiefly by distention, pain in the right lower quadrant of the abdomen and constipation over a period of 6 years. The past history was irrelevant except for rather frequent prolonged sore throats. There were occasional frontal headaches, but no dizziness, throbbing or tinnitus, and no symptoms referable to the urinary tract. The height was 66 inches,

the weight 171 pounds, the pulse 88, the temperature 99°F., the hemoglobin 88 per cent (Dare), and the blood pressure 128/82.

Physical examination revealed a well-developed and moderately obese, healthy-appearing male. Examination of the eyes and ears was normal. The nasal septum was deviated slightly to the left. The tonsils were red, swollen and ragged, and yielded purulent material on pressure. There was no submental, cervical, axillary or inguinal adenopathy. The heart was normal in size, with regular rhythm and no murmurs or thrills. The lungs were clear throughout, the abdomen soft to palpation, and the genitalia normal. The extremities and tendon reflexes were normal. A specimen of urine was clear, concentrated to a specific gravity of 1.024, was acid in reaction (pH 4.5) and contained no albumin or sugar; the sediment was normal. Blood Wassermann and Kahn tests were negative. The patient was given advice concerning the proper care of his intestinal tract and was told to have his tonsils removed when the infection in them had subsided.

In August, 1939, the chronically infected tonsils were removed. Six days after the operation, consolidative inflammatory changes developed in both lung fields, and the patient was hospitalized for 1 month. During the following year the patient was seen on several occasions for minor complaints, at which times the blood pressure was routinely recorded (Fig. 3).

On December 7, 1940, after an interval of 6 months during which he had not been seen, the patient again reported because of almost constant, pounding headaches and dizziness. There was also an intensification of the backache noted at the first interview. The physical examination was similar to that already recorded except that the tonsils were absent and the blood pressure was 170/100. The urine showed a specific gravity of 1.020, was acid (pH 5.5) and contained no albumin or sugar; the presence of an occasional red cell was suspected. Because of the patient's urgent request for relief of symptoms, he was given potassium thiocyanate (300 mg. daily) and phenobarbital (8 mg. four times daily). This brought marked symptomatic relief and was therefore continued throughout the ensuing period of observation and investigation, though it probably affected subsequent blood-pressure readings.

During the following month investigation was undertaken while the patient was ambulatory. A complete examination of the back by an orthopedist showed no abnormalities, but the following day the patient reported lameness in the right kidney region as a result. A neurosurgeon was also consulted, who observed slight but definite changes in the caliber of the retinal vessels, but found the neurologic examination entirely normal. Roentgenographic examinations of the back and the skull were normal. Urine examination was negative except for the presence of a faint trace of albumin. A phenolsulfonphthalein test of renal function showed 25 per cent dye excretion in 15 minutes and 55 per cent in 1 hour. An intravenous pyelogram showed normal excretion from the left kidney but none from the right. Cystoscopy was therefore performed by one of us (C. M.). Retrograde pyelograms revealed a large right hydronephrosis with apparent constriction of the right ureter near the ureteropelvic junction (Fig. 4). Multiple stone shadows were visible at the lower pole of this kidney. Urine from both ureters was sterile, and contained 0 to 5 red cells, 0 to 3

smooth muscle. After removal of the kidney the blood pressure returned to normal. This case is a human example of the principle involved in the application of Goldblatt's clamp. The case reported by us had almost complete obstruction of the right ureter. The combination of obstruction and limitation of elasticity in the capsule may well have contributed to limited vascular pulsations in this case.

The uncommon occurrence of cases of hypertension due to unilateral renal disease does not necessarily indicate that the mechanisms outlined occur with equal rarity. If there are proved unilateral cases, presumably there are bilateral cases that cannot be proved by nephrectomy. In view of the fact that there is less normal renal tissue to exert its protective effect, such cases may outnumber the unilateral ones.

It would be premature to draw conclusions about the etiology of essential hypertension. It is probable that the number of human cases of renal hypertension is larger than the sporadic reports of proved unilateral disease indicate.

SUMMARY

The experimental basis of renal hypertension is discussed. The renin mechanism in animals appears to be definitely established. There are isolated instances of renal hypertension in man. These cases may be due to the renin mechanism.

A case of unilateral renal disease with hypertension is reported. The blood pressure was followed for two years before the onset of hypertension and for one year after recovery, which was instituted by removal of the diseased organ. The specimen was unusual in that there was an extensive granulating perinephritis in addition to an almost completely occluded ureter.

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MEDICAL PROGRESS

THE MECHANISM OF HEART FAILURE AND RELATED STATES*

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ALTHOUGH heart disease and heart failure are among the commonest and most serious conditions that afflict mankind, the average doctor is inclined to accept empirically the symptoms and signs that occur, and makes little attempt to relate them to the actual physiologic disturbances of the circulation. This attitude is taken in spite of the fact that the heart and blood vessels constitute a physical system in which vital biologic processes are less important than in the functioning of many other organs. In recent years an impressive accumulation of experimental evidence has added to knowledge in this field, and has permitted cardiologists to buttress some of their theories and to discard others.

The lag in general understanding of the mechanism of circulatory failure is due in part to the highly specialized nature of many of the experimental methods employed; in part to the complicated theoretical considerations involved; and in large part, too, to the fact that many physicians, and even cardiologists, have in the past considered the heart to be an isolated organ and have not paid proper attention to the fact that the heart and the peripheral blood vessels are integral parts of the same system, and that manifestations of heart failure are to a large extent demonstrable only in the peripheral circulation. There is now enough clinical and experimental evidence so that all physicians should have at least a working knowledge of the dynamics of the circulation in heart disease and of the nature of circulatory failure; if they so relate the clinical findings exhibited by their patients they will be better doctors, for their interpretations of signs and symptoms will rest on a sound basis.

So much has been published in this field of medicine in the last few years that it is undesirable to cite a comprehensive series of references. Specific articles will be referred to only when they have appeared recently, and no attempt will be made to cover the field completely. Papers are cited which

will add to the understanding of the general practitioner concerning certain manifestations of heart disease and failure.

Mechanism of Congestive Heart Failure

Two outstanding theories have been advanced to explain the physiologic mechanism of congestive heart failure. One, the "forward-failure theory," holds that the manifestations of cardiac decompensation are caused in the main by an inadequate output of blood by the heart. This was the belief of Sir James Mackenzie and Sir Thomas Lewis, and represents the point of view maintained until recently by most English and American clinicians. The second, the "backward-failure theory" of heart failure, was first clearly expressed a hundred years ago by James Hope. In the simplest terms it attributes the phenomena of congestive failure to congestion in the vascular circuit behind the failing ventricle. This theory has been accepted by most French and German clinicians ever since Hope's day, and in the last few years has been increasingly adopted by American investigators.

The forward-failure theory is attractive because of its apparent simplicity. The heart being a pump, it might appear at first glance that heart failure consists merely of a failure of this pump to eject sufficient blood. It is now possible to test this explanation experimentally, since in recent years technics have been perfected that are accurate in estimating the cardiac output under various conditions, and many data are now available. No attempt will be made to describe or evaluate these methods, all of which have their limitations, but the results obtained through them are now sufficiently numerous and in close enough agreement to justify certain conclusions.

As regards the relation between cardiac output and heart failure, Harrison¹ concludes, "Persons with congestive heart failure may and often do have diminished circulatory minute volume, but this is not the essential cause of their symptoms." Others have taken issue with this statement. Altshule² believes that the fundamental defect in congestive failure is a cardiac output that is low in relation to the metabolic needs of the body and the venous pressure. With this viewpoint Stewart³ agrees. Subsequent to the publication of these monographs, McGuire and his co-workers⁴ dem-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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onstrated low cardiac outputs in 3 patients in heart failure with an increase during recovery, but in a fourth patient the more severe the failure, the higher was the output. In another study they⁵ found low volume flows in 19 of 20 decompensated patients. The same authors⁶ also presented evidence, that patients with congestive failure are unable to increase their cardiac output in response to exercise to an extent that is attained by normal persons. Espersen⁷ has reported finding normal cardiac outputs in 12 of 27 patients in heart failure, although Seymour et al.⁸ obtained low outputs during failure in all the 6 patients studied, and the outputs increased with clinical improvement. Starr,⁹ employing an entirely different technic, that of the ballistocardiograph, has presented results indicating that heart failure may occur with normal or even supernormal circulation. The validity of this method has not yet been fully demonstrated, but the results are certainly suggestive. It is also well known that heart failure may occur in conditions characterized by increased circulation (hyperthyroidism, arteriovenous aneurism, anemia and possibly beriberi). It would seem wisest, therefore, in the light of our present knowledge to echo what Starr says:

The majority of cases [of congestive failure] have subnormal circulations, and improvement in the circulation often coincides with clinical improvement. On the other hand, the relationship is not invariable, and any idea that the symptoms are the direct mechanical consequence of a diminished circulation must be abandoned.

In summary, therefore, our present knowledge suggests that the relation of cardiac output to heart disease and failure is as follows:

In compensated organic heart disease the resting cardiac output is often somewhat reduced, but may be normal or even increased.

In congestive heart failure there is usually a further decrease in cardiac output. The output per beat is especially apt to be impaired. When the output is considered in relation to the oxygen consumption of the body (basal metabolic rate) or to the venous pressure of blood reaching the heart, its diminution is even more evident. Nevertheless, the output is occasionally normal or even increased, either in absolute terms or relatively to the output before failure occurred. The degree of clinical failure does not bear any quantitative relation to the change in output.

With recovery from failure the output usually improves, but rarely to the point that existed before failure.

In the presence of heart disease, exercise increases the cardiac output less than normally;

and if congestive failure is present, the increase in flow is even smaller.

The cardiac output may be reduced in many conditions—acute or chronic—in which none of the signs of clinical heart failure are present.

A simple decrease in cardiac output is an inadequate explanation of congestive heart failure.

If, then, the clinical picture of congestive failure cannot be adequately explained by decreased cardiac output alone, what is the causative mechanism? The answer is to be found, not in the outflow of blood from the heart, but in the inflow into the auricles and ventricles. Twenty to thirty years ago, Starling and his associates^{10,11} carried out a brilliant series of investigations on cardiac physiology, and found that an increase in stretching—that is, dilatation—of the muscle, is accompanied by an increase in the strength of contraction; that the venous pressure is the important factor in controlling this diastolic stretching and hence the cardiac output; and that the rate of metabolic processes of the heart muscle is determined by the length of the fibers rather than by the work accomplished (that is, a dilated heart consumes relatively more oxygen than a normal one).

According to the backward-failure theory of congestive failure, the diseased heart is inefficient, requires a greater venous pressure and hence more dilatation in order to effect a given output of blood, and uses up more energy—that is, consumes more oxygen—in doing so. This results in more and more cardiac dilatation, with an increasing amount of residual blood left in the ventricles in diastole. The presence of this residual blood produces effects transmitted back to the auricles and to the great veins so that blood under increased pressure piles up in the vascular circuit,—either pulmonary or systemic,—and this congestion initiates the train of circumstances that produces the characteristic symptoms of heart failure—dyspnea, edema and so forth. Since in the vast majority of clinical types of heart disease the left ventricle is subjected to greater strain than is the right, it usually fails first, and it is the pulmonary circuit that is engorged. Eventually the strain that this vascular congestion and hypertension impose on the ventricle that has not failed proves too great, and this ventricle in turn fails.

In the controversy that has existed between the backward-failure and forward-failure exponents, one point is not infrequently overlooked which to some extent reconciles the two viewpoints. This is that blood normally must be simultaneously pumped by both ventricles in exactly equal amounts. If one ventricle ejects less than the other, even by a minute amount or for a few beats, blood

tends to pile up in the vascular circuit behind the impaired ventricle, until the venous pressure is sufficiently raised to act as a stimulus for an improved ventricular discharge. Such small and relative changes in volume flow from the two sides of the heart cannot be measured in human beings by any available method, but it is probable that they play a significant role in the pathogenesis of congestive failure, and possibly in the exertional dyspnea of persons with limited cardiac reserve.

Further consideration concerning how back pressure and congestion behind a failing ventricle can lead to clinical manifestations, together with the many secondary factors that contribute to the aggravation of the symptoms, will now be discussed.

Dyspnea

Dyspnea is the cardinal symptom of left ventricular failure and is explainable by the sequence of vascular events described above occurring in the pulmonary circuit. With dilatation of the left ventricle and increase in pressure in the pulmonary veins, there ensues an increased pressure transmitted back into the pulmonary capillaries, with resultant engorgement of these vessels and ultimate exudation of fluid into the alveolar spaces. Consequent on these changes the lungs are stiffened by the dilated, engorged vessels, the vital capacity is diminished, and the residual air is increased. It is known that the respiratory reflex that alternately initiates inspiration and expiration (Hering-Breuer reflex) is dependent on the degree of stretching or stiffening of the lung, and that in experimental animals in which sudden pulmonary vascular engorgement is produced rapid, shallow breathing results.¹² The distressful, rapid, shallow breathing that occurs in clinical heart failure is therefore due in large part to this reflex effect occasioned by the pulmonary congestion. Other factors may play a role, but probably not an important one, except in advanced heart failure or during exercise. Such factors are arterial anoxemia caused by impairment in the pulmonary exchange of gases, and central effects on the respiratory center as a result of failure of an adequate circulation in providing oxygen or removing carbon dioxide or other acid metabolic products.

The cause of paroxysmal cardiac dyspnea is not fully established, but no better explanation has been given than that of Weiss and Robb.¹³ In brief, according to their theory the cause is acute left-sided failure, precipitated by one or more trigger mechanisms, all concerned with the inadequacy of the horizontal as compared with the elevated position of the thorax. These advantages of the elevated thoracic position are mechanical factors aiding breathing, decrease in the hydrostatic element

of both peripheral and pulmonary venous pressure, and a slight and possibly inconstant decrease in cardiac output. In addition, when a cardiac patient assumes the recumbent position after having been up and around during the day, there may be a well-marked increase in plasma volume due to the mobilization of extravascular fluid. This added circulatory burden was suggested by Weiss and Robb, but it remained for Perera and Berliner¹⁴ to demonstrate it unequivocally in cardiac patients subject to paroxysmal dyspnea.

A possible role of neurogenic reflexes in the precipitation of these attacks was also brought out by Weiss and Robb. However, that such a role is contributory only is the belief of the majority of investigators.

Edema and Diuresis

Until comparatively recently the explanation of edema of cardiac origin seemed to be simple. Since there is an increased pressure in the peripheral veins in right-sided heart failure, it was logical to assume that this heightened pressure is conveyed back to the capillaries, thus increasing the hydrostatic pressure and the tendency for more fluid to be driven into the tissue spaces. Fahr and Ershler¹⁵ have shown that edema is likely to form when the hydrostatic pressure at the venous end of the capillary loop rises to within 2 mm. (mercury) of the colloid-osmotic pressure of the plasma. However, the complexity of the factors contributing to edema formation is becoming increasingly evident, as Altschule² has brought out, and he has shown that the degree of edema does not bear any absolute relation to the height of the venous pressure. Several elements enter into the control of the level of pressure in the venous system. Not only is the ability of the heart to pump forward the blood reaching it important, but peripheral conditions modify the pressure level. The degree of constriction of the blood vessels in various parts of the vascular circuit is one prominent factor. A lowered venous tone tends to lower the venous pressure; increased arterial tone with a normal venous tone tends to shunt blood into the venous channels, and hence to increase the venous pressure. The total volume of circulating blood also plays a vital role, as has been brought out by Bazett.¹⁶

It has been shown^{8, 17, 18} that the blood volume is often increased in heart failure, especially that of the chronic right-sided type. The assumption has frequently been made that this increase in plasma volume is the result of the train of circumstances consequent on a high venous pressure and an increase in the peripheral vascular bed, and that with improvement and the onset of diuresis this

train of events is reversed; that is, the venous pressure falls owing to improved cardiac action, the plasma volume decreases because of better renal activity as the result of improved renal blood flow or the effect of diuretics, and fluid returns to the blood stream from the tissues and is excreted. However, a number of recent observations do not conform to this simple explanation. Stewart¹⁹ found evidence that the plasma proteins fall with the onset of diuresis, suggesting that fluid enters the blood stream to dilute the plasma *before* diuresis commences. Swigert and Fitz²⁰ also found the plasma volume sometimes increased after giving a mercurial diuretic, as though the fluid were first mobilized from the tissue, before renal excretion took place. Calvin, Decherd and Herrmann,²¹ however, found such an increase in only 2 cases following the administration of Salyrgan, and in these patients diuresis was delayed or failed to occur. In 13 other cases where prompt diuresis took place the plasma volume diminished. Of significance, too, is the observation of Fletcher and Schroeder²² that some patients with cardiac edema apparently have a specific tendency to retain sodium and that their loss of edema fluid follows a change in the sodium balance. Warren and Stead²³ are of the belief that edema develops in congestive failure because the renal excretion of salt and water is altered by a decreased cardiac output, and that this increase in extracellular-fluid volume is accompanied by an increase in plasma volume that eventually causes a rise in venous pressure. Support for the thesis that a rise in venous pressure follows an increase in plasma volume is to be had in the work of Starr,²⁴ who showed that the pressure in the veins and other parts of the vascular circuit after death of patients dying in congestive heart failure is markedly higher than in those dying of other causes. He interpreted this as possibly due to an increased blood volume that overloads the vascular system.

It has not yet been conclusively shown in what way the venous pressure, as measured in the usual fashion in the antecubital vein, reflects the pressure in the capillaries on the one hand and in the right auricle on the other. There is evidence that normally the antecubital venous pressure is higher than that in the right auricle by several centimeters of water,²⁵ but this gradient is abolished in patients and experimental animals with right-sided heart failure and elevated venous pressure.

The explanation for these various observations, at variance with the usual concept of edema formation and diuresis, is not entirely clear, but it has been suggested by Schroeder and by Warren and Stead that hormonal influences may be involved

in the retention of electrolytes. It is well known that the hormones of many of the endocrines exert some antidiuretic effect²⁶ and that actual heart failure in patients with Addison's disease may be precipitated by an overdosage of desoxycorticosterone,²⁷⁻³⁰ owing to excessive sodium retention and increase in plasma volume.

Thus the exact relations and the causal connections between the level of venous pressure and the degree of heart failure remain unsolved problems. It is not unlikely that a vicious circle is established whereby right-sided heart failure produces vascular congestion and a tendency toward increase in pressure in the systemic venous reservoir. This in turn initiates a sequence of events that may maintain or further elevate the pressure regardless of the cardiac status itself. These other factors affecting edema formation deserve consideration.

Landis and Gibbon³¹ and Sodeman and Burch³² have pointed out the importance of tissue pressure in controlling edema formation. Persons with firm, elastic subcutaneous tissues accumulate edema much less readily than do those whose tissues have lost their elasticity and are readily stretched, such as old people and those who have lost weight or who have previously been edematous.

The role of a lowered plasma osmotic pressure in cardiac edema has also come in for a good deal of study, and it is now well known that the plasma proteins and especially the albumin fraction may be significantly lowered. Several factors may contribute to this lowering: impaired intake of protein; deficient absorption; increased loss through the kidneys, into serous effusion or into edema fluid itself; defective formation due to hepatic congestion; and hydremia or increase in plasma volume without a concomitant increase in plasma protein. The lower the plasma osmotic pressure from whatever cause, the less the increase in hydrostatic pressure that is required to initiate edema formation.

Another factor that may play a part in edema formation is capillary anoxemia, which causes dilatation and increased permeability of the capillaries. Smirk's³³ experiments indicate that such anoxemia is important in the production of cardiac edema, but Fahr and Ersler¹⁸ are of the opinion that it plays little or no part. The fact that the protein content of cardiac edema fluid is low, averaging less than 0.5 per cent, indicates that increase in capillary permeability does not progress to a point permitting the passage of protein in high concentration.

Lymphatic drainage from the
has been shown to occur in patients with

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, MD, *Editor*

CASE 29091

PRESENTATION OF CASE

A twelve year old boy was referred to this hospital with a diagnosis of pneumonia.

Three days prior to admission the patient complained of epigastric pain and on the next day ate poorly and did not seem well. However, there were no other signs or symptoms. On the day prior to admission he vomited ingested food and his temperature was elevated to 103°F. His physician found signs of consolidation in the right lung, and because of fever, 2 gm. of a sulfonamide drug was administered. On the day of admission he developed a hacking nonproductive cough. At no time had he experienced chills.

The family history was noncontributory. For three and a half years the boy suffered with repeated attacks of otitis media and mastoiditis necessitating bilateral drainage of the middle ear and resection of the mastoid cells on the left side. Three years before entry, because of a suspected brain abscess, an exploration was made through the right temporal bone; no abscess was found. Six months previously, because of recurrent pain in the left mastoid area and profuse drainage of pus from the ear, mastoid resection was revised. He was treated with a course of orally administered sulfadiazine totaling 46 gm. in nineteen days. *Staphylococcus aureus* and a beta hemolytic streptococcus were cultured from the pus.

Physical examination revealed an acutely ill, cyanotic, obese boy. Respirations were rapid and shallow, and there was an occasional hacking nonproductive cough. The mucous membranes were congested and dry. The heart was normal. The right chest was dull from the midscapula to the base. Bronchial breathing and bronchophony were prominent throughout the right chest posteriorly in the axilla and to a less marked degree anteriorly at the base. The abdomen was soft, and no masses were felt.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 105°F, the pulse 90, and the respirations 60.

The white cell count was 26,000. The urine was acid, had a specific gravity of 1.015 and gave a +++ test for albumin; the sediment contained an occasional white cell, an occasional red cell and many hyaline and granular casts.

A chest roentgenogram taken in the horizontal position showed increased density throughout the greater portion of the right lung field more marked in the medial two thirds of the lung. The density had a ground glass appearance and was more marked at the base. The heart was slightly displaced to the left. The left lung was not remarkable. No pyothorax were grown from the sputum, and only obvious contaminants were found in the blood culture.

Despite the intravenous administration of 10 gm. of sodium sulfadiazine during the first day, producing a blood level of 15.6 mg. per 100 cc, the boy became increasingly restless and disoriented. The pulse rose above 120, and he died approximately thirty hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON. In the first place, I am sort of hipped on blood smears, and I should like to comment that with a white cell count of 26,000 in a boy with a temperature of 105°F, and findings in the chest, a good deal of stress might justifiably be laid on the type of blood picture. The white cell count was done in the Emergency Ward, and no differential count is given anywhere in the record. I should suspect it showed 94 per cent polymorphonuclears, 6 per cent lymphocytes, no eosinophils and no monocytes. On the other hand, because nothing is said about the differential count, perhaps we can accept it as normal—that is of great significance. I doubt if it was. I should also guess that the boy had a red cell count of 3,500,000 with a hemoglobin of 11.6 gm.

The questions I should ask in regard to this boy are: Did the previous sepsis have anything to do with the present illness? Did the boy have pneumonia? Did he have empyema? And finally, did he have amyloid disease or did he have nephritis of some type? These are the questions I have to answer, but I am not sure that I am going to be successful.

In the first place, did the previous sepsis have anything to do with the immediate illness? My inclination is to suspect a pneumonic process which had nothing to do with the previous mastoid infections. In other words, I think he did have pneumonia on the evidence here submitted. I suspect the presence of pneumonia from the history of the onset and from the physical findings. The question is, Were the physical findings

definitely those of consolidation or could they have been those of fluid and compression of the lung?

Whether he had empyema or not, I am not sure. If it was empyema, one would be surprised to find such definite evidence of it so soon in the course of the recent illness. One would have to believe he had had it for some time.

Finally, in regard to his kidneys, there was a moderate reduction in the specific gravity. There was a large amount of albumin, which is greater than I should expect with a temperature of this degree, especially when it was associated with a gravity that was somewhat low. If it were not for the granular casts I should be thinking definitely in terms of some type of nephrosis—especially amyloid disease, because of the previous sepsis. I do not see how I can rule amyloid disease out or in on the basis of this history. The questions are whether he had amyloid disease of the kidney, whether he had subacute nephritis or whether the renal damage could be attributed to a reaction from sulfadiazine, which was given six months before entry for a course of nineteen days. I have not heard of any cases of kidney disease that progressed for six months after the cessation of the use of sulfadiazine or any of the sulfa drugs. I should say he had either subacute nephritis or amyloid disease and I shall make final diagnoses of pneumonia, chronic suppurative mastoiditis and kidney disease, possibly amyloid in nature.

I have not looked at the x-ray films. Dr. Mallory intimated to me that Dr. Schatzki was particularly interested in them. I should think I might be allowed to look at the plates first, and Dr. Schatzki can discuss them afterward.

This film was taken with the patient in the horizontal position and the question comes up, Was this one of those cases of so-called "localized edema" of the lungs associated with renal disease in which Dr. Mallory thinks that there is some sort of a consolidating process? Am I wrong in saying that?

DR. TRACY B. MALLORY: I am still uncertain what that lesion really is. In such cases, the lungs usually appear more hemorrhagic than edematous.

DR. RICHARDSON: I do not know much about x-ray films, and I shall not go out on a limb on that diagnosis in this case. I want to mention it knowing that Dr. Schatzki is going to talk about these films. From this film, I cannot rule out the possibility of fluid in the right chest. The heart seems to be pushed somewhat to the left. I am going to put in a question of empyema in addition.

DR. RICHARD SCHATZKI: This case was presented to the X-ray Department from the Emergency Ward with a clear-cut diagnosis of lobar pneu-

monia. For several reasons, the dangers in the chest looked somewhat different roentgenologically from those of the common variety of lobar pneumonia. The area involved was rather large but not dense. It had a translucent, ground-glass appearance, as the record states, apparently owing to alveoli that were not yet involved by the process. The medial portions of the lung were much more involved than the peripheral one. All this made us think that it might well be a localized pulmonary edema. We could not rule out pneumonia, in addition to the pulmonary edema. We certainly thought that the kidney should be checked. This was done, resulting in the findings that are mentioned.

DR. WILLIAM B. BREED: Dr. Richardson, I suggest that the person who abstracted this record perhaps took a little too much on himself in the last paragraph when he said, "Despite the intravenous administration of 10 gm. of sodium sulfadiazine during the first day, producing a blood level of 15.6 mg. per 100 cc., the boy became increasingly restless and disoriented. I suggest that he might have said "because of." That is a high blood level, and the boy had had a large amount of sulfadiazine six months previously. I am not sure that the treatment was not a factor in his rather sudden demise.

DR. RICHARDSON: Fifteen milligrams does not seem to be an unusual level. It is frequently attained without serious toxic symptoms.

DR. ALLAN M. BUTLER: Was the 10 gm. given intravenously at one time? I think that is a lot.

DR. MALLORY: It was divided into at least two doses.

DR. BUTLER: How far apart?

DR. MALLORY: It was spread over twenty-four hours. There is no further comment.

DR. BUTLER: Before we hear the diagnosis, I should like to ask Dr. Schatzki if there is prominence of the right border of the heart at the base.

DR. SCHATZKI: No; I think it is normal considering the conditions under which the film was taken.

DR. FULLER ALBRIGHT: This boy was in the hospital about twenty-four hours. I saw him in an oxygen tent, and he was obviously extremely sick. To me, he obviously had a pneumonia. The localized edema of the lungs that Dr. Schatzki has mentioned would be most unusual. The only question in my mind was whether he had acute cardiac failure. We felt sure it was pneumonia. We did not get a differential count, which was unfortunate. It might have given a clue.

DR. BUTLER: There were many hyaline and granular casts in the urine. I do not know whether the boy was dehydrated or not.

DR. ALBRIGHT: The high fever and passive congestion could explain these. One certainly observes casts with high fever.

DR. BUTLER: Yes, but the specific gravity was only 1.015, which means the urine was not concentrated. With high fever, casts and red cells in the urine are usually associated with a concentrated urine.

DR. ALBRIGHT: That is true, but I must confess that I am not disturbed about it.

DR. MALLORY: I shall describe the anatomical findings and then ask Dr. Schatzki to speak again.

CLINICAL DIAGNOSES

Lobar pneumonia.

DR. RICHARDSON'S DIAGNOSES

Chronic suppurative mastoiditis.

Pneumonia.

Kidney disease (? amyloid).

Empyema?

ANATOMICAL DIAGNOSES

Acute glomerulonephritis.

Subacute mastoiditis.

Pulmonary edema.

Pneumonia.

Operative scar: decompression wound.

Focal encephalomalacia, old, inactive.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy this boy had large, distended and heavy lungs. The peripheral portions of the lungs in all lobes were well aerated, whereas the central portions were practically consolidated, with obviously a great deal of fluid in the alveoli. The lungs did not show any granular foci. Our impression in gross was that this was a massive degree of pulmonary edema centralized in the hilar regions and not present in the peripheral portions of the lung. The kidneys were of normal size. When sectioned, the cortices seemed paler than normal and bulged a little bit over the capsule, but in gross we could not be certain of nephritis. The sections, however, show an obvious acute intracapillary glomerulonephritis. The sections of the lungs are much more difficult to interpret. They look frankly pneumonic, with a great many leukocytes and some fibrin, but also a good deal of free fluid and a great many red cells. It is well within the limit of possibility, and as a matter of fact I think it probable, that these lungs were edematous at first and became pneumonic terminally—in other words, that the pneumonia was secondary rather than primary. However, I cannot prove that on histologic grounds.

I think all of us have been impressed with the way Dr. Schatzki looks at a chest plate and often diagnoses nephritis. All of us have seen him do it too often for it to be pure coincidence. I am convinced that there is something in it. The nature of this pulmonary lesion is difficult to explain. It is different from the ordinary types of pulmonary edema that we see in other conditions. Pulmonary edema usually takes one of two forms. In one, there is an obviously wet lung. Frothy fluid bubbles from the bronchi when you press on the lungs, and pours in abundance from cut surfaces of the pulmonary parenchyma. That is what one sees with acute heart failure and with so-called "cardiac asthma." In the other type of pulmonary edema the fluid is not readily expressed by pressure. It seems to be of a gelatinous consistency, and when the lung is fixed it is precipitated as a diffuse colloidlike sheet in the alveoli rather than as granular detritus. In either type small numbers of red cells may be found in the alveoli. The lesions in the group of nephritic cases that Dr. Schatzki has been interested in do not look like those of either type of ordinary edema. The gross appearance of the lung is that of scattered hemorrhages, and microscopic examination always shows more obvious hemorrhage than edema. There is always fluid as well, but the red cells are so numerous that they predominate the picture. There is apt to be some fibrin, and there may or may not be leukocytes. In this case there were so many leukocytes that if I did not have the history, I should have passed it over as ordinary pneumonia.

A PHYSICIAN: A fatal course in twenty-four hours is extremely unusual for pneumonia. Furthermore, a pneumonia involving all five lobes is rare in the absence of a predisposing factor. What does the negative culture mean?

DR. MALLORY: I do not know. I wish we had been more impressed with the idea of pneumonia at the time of death and had cultured the lungs more carefully than we did. Certainly, the negative sputum makes me suspicious that it was not the usual pneumococcal pneumonia.

DR. SCHATZKI: The post-mortem film of the chest is interesting. It looks practically like that of a stillborn baby. There is barely any air in the lungs. The right lung has none, but there is a little in the periphery of the left lung, as you can see. It seems to me that the coincidence of these pulmonary lesions with nephritis, as Dr. Mallory points out, is too common to be laughed off. In some of these cases the films of the chest look exactly like those of cases of pulmonary edema of cardiac origin; the changes are bilateral and fairly symmetrical. In others, the pulmonary le-

sion is asymmetrical and less characteristic. The roentgenologic picture, as well as the clinical course, is not that of pneumonia.

DR. MALLORY: Would you be able to distinguish the picture from so-called "rheumatic pneumonia," Dr. Schatzki?

DR. SCHATZKI: I have not seen many cases of rheumatic pneumonitis. The films in these few cases showed changes that looked roentgenologically like those of localized pulmonary edema, and the patients acted much the same. From talking with you, Dr. Mallory, and with Dr. Bland, I have been impressed that these two conditions are also similar histologically.

DR. MALLORY: I am inclined to think that the histologic picture is the same in certain cases.

DR. FLETCHER H. COLBY: Is there any possibility that the previous sulfadiazine had anything to do with the picture?

DR. MALLORY: This was acute glomerulonephritis, and there was no sign of sulfadiazine involvement. The process was acute and had not reached a stage where the boy would have died of renal insufficiency if he had not had the pulmonary complication.

DR. RICHARDSON: Did he have fluid in the chest?

DR. MALLORY: Only 6 or 7 cc. on each side.

DR. ALBRIGHT: May I ask Dr. Schatzki a few questions? I want to be sure I understand this. In certain cases of kidney disease, is there edema in the lungs that is not due to low serum protein, not due to generalized anasarca, and not due to hypertension and cardiac failure? What is it? Can you be sure it is not caused by pneumonia?

DR. MALLORY: It might be a sterile pneumonia like the sterile pericarditis one sees in uremia. Other well-known inflammatory lesions in uremia are, of course, colitis and gastritis. This may be a pulmonary manifestation of the same type of capillary injury.

DR. ALBRIGHT: In other words this is a pneumonia for which you can find no bacteria. I cannot see why you cannot get acute pneumonitis from the same bug that is causing the trouble in the kidney; that is, the same process is going on in the lung as in the kidney.

DR. MALLORY: For one thing the streptococcus is not found in the kidney, and you do not ordinarily find streptococci in these lungs. However, the problem is difficult to solve with post-mortem studies since edema fluid is an ideal culture medium and so many organisms grow luxuriantly in it that mixed cultures are the rule and are often impossible to interpret.

DR. SCHATZKI: A few facts are difficult to fit in with your theory, Dr. Albright. A number of

these patients did not have acute glomerulonephritis, but chronic or subacute glomerulonephritis. In some of them, the pulmonary lesions developed simultaneously with generalized anasarca.

DR. ALBRIGHT: Localized edema of the lung and generalized anasarca?

DR. SCHATZKI: In addition, a number of patients showed no clinical evidence of infection. Furthermore, in several cases at autopsy the histologic picture was not that of pneumonia but that of hemorrhage.

DR. ALBRIGHT: Hemorrhagic exudate?

DR. MALLORY: Yes; it looked as if the capillaries let red cells through instead of merely fluid.

A PHYSICIAN: No white cells?

DR. MALLORY: Only a small number such as you might expect in proportion to the red cells.

DR. JOSEPH AUB: You call this "localized edema." What is the evidence of this edema?

DR. SCHATZKI: It has the roentgenologic appearance of localized edema as seen occasionally in pulmonary edema of cardiac origin. The picture is more obvious in cases with symmetrical bilateral pulmonary edema.

DR. MALLORY: Have you not had some cases with acute nephritis in which the x-ray picture cleared up with dramatic suddenness in twenty-four hours?

DR. SCHATZKI: That is right. It is rather hard to connect that with pneumonic consolidation.

DR. BUTLER: To me there is something odd about this patient, if he had acute glomerulonephritis.

DR. MALLORY: It is a frequent sequel of mastoid disease.

DR. BUTLER: Yes, but these patients do not die of uremia and acute glomerulonephritis in a course of three days.

DR. MALLORY: We are not claiming that he did, Dr. Butler.

DR. BUTLER: All right. Then if his death was due to nephritis, he ought to have had either cardiac failure with hypertension or a crisis of hypertension earlier, in the first few days of the acute process. He had diminished concentration of urine, and it seems to me that the story and findings are not consistent with death and acute hemorrhagic nephritis.

DR. MALLORY: The patient died because he could not breathe, died because of his lung condition.

DR. BUTLER: How often do you find that in the lungs without hypertension or cardiac failure or without uremia?

DR. MALLORY: One can have acute cardiac failure in nephritis without hypertension, according to Longcope.*

DR. BUTLER: Yes, but there is nothing in the physical examination to give evidence of cardiac failure.

DR. ALBRIGHT: We thought clinically that there was a possibility of cardiac failure.

CASE 29092

PRESENTATION OF CASE

A twenty-seven-year-old housewife came to the Out Patient Department of the hospital because of pain in the right lower quadrant of the abdomen.

Approximately five years prior to admission the patient noted the onset of attacks of nonradiating pain in the right lower quadrant of the abdomen. This was usually knifelike but occasionally was crampy and caused her to double up. These attacks usually lasted about an hour and were relieved by bed rest. The pain often occurred every two or three weeks but bore no apparent relation to the menstrual cycle. Simultaneous with the episodes of pain a mild leukorrhea developed, but the patient denied any exposure to venereal infection. Between attacks the patient had a constant dull ache in the right lower abdomen. There were no gastrointestinal symptoms associated with the illness. For the past several months she had had nocturia two or three times every night.

The family history was noncontributory. The patient had had a normal child eleven years previously. At about the same time her first husband died of pneumonia, and she remarried four years later. Although both she and her husband desired a child, no pregnancies had occurred.

Physical examination disclosed slight tenderness in the right lower quadrant of the abdomen, but no mass was felt. There was some thickening of the left broad ligament, and a 4-cm. tender mass was felt in the right vault that seemed connected with the fundus of the uterus. There was a slight erosion of the cervix, with a profuse vaginal discharge. A cervical smear and culture were negative for the gonococcus.

The urine was acid and had a specific gravity of 1.030; the sediment contained an occasional red cell, 7 white cells and 15 epithelial cells per high-power field.

The patient was started on sulfadiazine and warm vaginal douches, and was told to rest in bed. During the next two weeks, the discomfort gradually improved and the vaginal discharge was re-

duced. The right adnexal mass seemed to persist but was only slightly tender. After two weeks the sulfadiazine was discontinued but the patient was instructed to continue the warm vaginal douches. Several days later she had a sudden attack of crampy pain that caused her to double up. Ice packs applied to the abdomen temporarily relieved the pain but she continued to have a steady dull ache in the lower abdomen. She was then admitted to the ward.

The menarche started at fourteen and the periods were always regular, with a twenty-eight-day cycle, and lasted three days, with no pain. The last catamenia began five days before she entered the hospital.

Physical examination revealed a well-developed young woman in no obvious distress. Examination of the heart and lungs was negative. There was marked tenderness to direct pressure in the right lower quadrant of the abdomen. No rebound tenderness could be elicited, and no masses were felt. On vaginal examination there were definite tenderness and thickening in the right vault. One examiner described a moderately tender right adnexal mass about the size of a small orange. The cervix was lacerated and seemed soft. The uterus was slightly enlarged and was freely movable. A small amount of white discharge was present in the vagina. There was tenderness on the right side of the rectum.

The blood pressure was 124 systolic, 85 diastolic. The temperature was 98.6°F., the pulse 80, and the respirations 20.

The examination of the blood revealed a hemoglobin of 95 per cent and a white-cell count of 10,000. The urine was negative. A blood Hinton test was negative.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. FRED SIMMONS: Many of the data presented in the record may have no time relation to the incident that led the patient to undergo surgery, since there was an undefined interval between the time she was seen in the Out Patient Department and in the ward. The history tells us that eleven years before entry she had a child and that at the time of entry she was only twenty-seven. So she must have been married at fifteen, and her husband died at about the time the infant was born. She went four years without the possibility of pregnancy and then remarried. Seven years elapsed during which she presumably tried for a child but did not secure one. These data lead one to suspect an inflammatory process in the genital tract. However, I should like to point out that

*Nicholls, M. R., Longcope, W. T., and Williams, R. Occurrence and significance of myocardial failure in acute hemorrhagic nephritis. *Bull John Hopkins Hosp.* 64:83-113, 1937.

it is becoming increasingly important to consider the male partner in any question of sterility. There is no mention of the husband here.

The urinary tract reveals the possibility of disease. She had nocturia two or three times. The recorded urine probably was not a catheterized specimen and therefore the findings are not entirely reliable. But it is of some significance that there were occasional red cells, 7 white cells and 15 epithelial cells per high-power field. This case reminds me of a girl who had abdominal pain, with little in the line of urinary symptoms. Palpation revealed a slightly tender mass in the left vault the size of an English walnut or perhaps larger; x-ray studies revealed a sac full of stones. She was cystoscoped and a slight slit made in the left ureter produced twenty-seven stones. She had a ureteroceles at the base of the ureter where it joined the bladder. That could be the case here.

The pelvic examination in the Out Patient Department was undoubtedly made by a different examiner from the one on the ward. Therefore the 4-cm. tender mass felt by the former and the orange-sized mass felt by the latter could be the same. One examination was made when the patient was in pain, and the other when she was not. One examination was perhaps made by a house-officer, and the other by a visiting man. I cannot be sure but I should like to think for the purpose of what I am going to say later on that there was a change in size in the mass. The leukorrhea in relation to these episodes of pain and the fact that she had a profuse vaginal discharge are rather pertinent even if the cervical smear and culture were negative. As you all know, in the acute stage of a Neisserian infection of the adnexa, culture or smear may fail to show organisms.

The situation before admission to the ward certainly sounds like pelvic inflammatory disease, probably bilateral, with almost certainly a right salpingitis.

We learn from the history that the menarche started at fourteen and that the periods were always regular, with a twenty-eight-day cycle, and lasted three days, with no pain. The last catamenia began five days before the patient entered the hospital.

Since she had been having abdominal pain for at least a week before entry, it must have continued throughout the menstrual period. The fact that the patient had had this period allows me to rule out all complications of pregnancy—

ectopic gestation, early abortion and all that sort of thing.

Tenderness on the right side of the rectum suggests diseases of the gastrointestinal tract. I believe one should mention in the differential diagnosis appendicitis, appendiceal abscess, mucocele and Meckel's diverticulum. Another possibility is dermoid cyst, of which we see ten or twelve cases a year in this hospital. Many are unilateral. The bilateral ones are frequently picked up only by pelvic examination, or demonstrated by x-ray, especially if they have teeth in them. Another possibility that should be considered but that can be ruled out by the menstrual history is a ruptured corpus hemorrhagicum. If this attack had occurred midway in the cycle, between the twelfth and twentieth days, such a diagnosis would have to be thought of. The patient could have a persistent corpus luteum—a frequent cause of sterility.

It is obviously impossible to make an exact diagnosis on the data presented. I shall make a diagnosis of pelvic inflammatory disease, with possibly a twist of a hydrosalpinx.

CLINICAL DIAGNOSIS

Pelvic inflammatory disease.

DR. SIMMONS'S DIAGNOSES

Pelvic inflammatory disease, bilateral.
Right hydrosalpinx, with torsion?

ANATOMICAL DIAGNOSIS

Dermoid cyst of ovary.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: When this patient was explored a large yellow cystic mass was found in the right ovary. Both tubes were entirely normal and so was the appendix. The ovarian mass was removed and proved to be a dermoid cyst full of cheesy material and hair; it contained no teeth, bone or any structures that would have been shown by x-ray examination. Nothing was discovered to account for the acute attack of pain that brought her into the hospital on the last occasion. There was no twisted pedicle or any other lesion to explain why this cyst, which evidently had been present for some years, should have suddenly produced symptoms.

DR. SIMMONS: Was the mass the reason for operation?

DR. MALLORY: Yes; the preoperative diagnosis was the same as yours—pelvic inflammatory disease.

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NEW AGENTS IN THE TREATMENT OF INFECTIOUS DISEASES

THE search for new weapons is a part of modern warfare, and there is no denying the fact that the development of new weapons to aid in the defeat of bacterial infections is well under way. Every physician is familiar with the phenomenal results that have been achieved from the use of the sulfonamides, and now other agents are being discovered, that may be useful in the treatment of infections that fail to respond to the sulfonamides. Among those under investigation at present are the so-called "antibiotic" agents—that is, substances that destroy or so modify biotin that it cannot be used by bacteria for their normal growth.

It has been known for many years that certain bacteria, such as *Pseudomonas pyocyaneus*, elaborate substances that are inhibitory as well as lethal to bacteria. Fleming,¹ in 1929, described a soluble substance, "penicillin," which he obtained from the growth of *Penicillium notatum*, that inhibited the growth of gram-positive organisms in vitro. It was nontoxic to animals when given in relatively large quantities, and it was used by him for the local treatment of ocular infections.

A few years later Dubos and Avery² described an enzyme that was obtained from the growth of a bacillus obtained from soil and that was capable of removing and destroying the capsular material of the Type 3 pneumococcus. Other enzymes were derived from bacteria that would act the same way with several other types of pneumococci. Later, Dubos³ isolated a substance from another species of soil bacillus, *Bacillus brevis*; it was called "tyrothricin." This material is bactericidal for gram-positive organisms and can be separated into two fractions—"gramicidin" and "tyrocidine." Other antibiotic agents have been described recently and include "glyotoxin," "actinomycin," "citrinin" and "aspergillin." Of all these agents, tyrothricin and penicillin have been studied most intensively. In a recent number of *War Medicine*, Rammelkamp⁴ summarizes the results that he obtained with tyrothricin in the treatment of infections. Reports on the use of penicillin are beginning to appear from England (Florey and his associates⁵) and from the United States (Dawson and his colleagues^{6,7}).

It is now clear that tyrothricin can be used locally for the treatment of ulcers of the skin, of wounds of the mastoid process and of empyema due to infection with staphylococci, streptococci and pneumococci. Since the material is relatively insoluble except in alcoholic solution and since it does not penetrate the tissues following local application, its use must be confined to the topical treatment of infections. It cannot be given intravenously because of its toxic reactions; there is, however, no evidence that the material is absorbed from local areas of infection since no signs of intoxication follow its topical use. Further studies

MEDICAL EPONYM

STRÜMPEL-MARIE DISEASE

Adolph Strümpel (1853-1925) in the second volume of the first edition of his *Lehrbuch* (Leipzig, 1884, page 152) described this peculiar form of chronic arthritis. A portion of the translation follows:

Those forms may here be mentioned in passing as a remarkable and, as it seems to us, a distinct disease in which there results a gradual and painless complete ankylosis of the vertebral column and hip joints so that the head, the trunk and the thighs are firmly united to each other and become completely stiff, while all the other joints retain their normal mobility. It is apparent that a characteristic modification of the posture and gait must occur as a result. We have seen two quite similar cases of this peculiar disease.

He discusses the entity in more detail in an article, "Bemerkung über die chronische ankylosierende Entzündung der Wirbelsäule und der Hüftgelenke. [A Note on Chronic Ankylosing Inflammation of the Vertebral Column and Hip Joints]." It was published in the *Deutsche Zeitschrift für Nervenheilkunde* (11: 338-342, 1897) as a comment on the preceding article on the same subject by Bechterew.

Pierre Marie (b. 1853) wrote "Sur la spondylose rhizomélitique [Rhizomelic Spondylosis]" in the *Revue de médecine* (18: 285-315, 1898). A portion of the translation follows:

In the session of February 11 of this year, I presented to the Société médicale des Hopitaux two patients afflicted with a disease whose symptoms, identical in both cases, seemed to me to be sufficiently interesting to be brought to the attention of clinicians. In this preliminary discussion, I indicated the principal characters of this disease entity and particularly stressed the extremely marked rigidity of the spine and the more or less complete ankylosis of the coxofemoral and scapulohumeral joints. Calling attention to the fact that the articulations of the roots of the extremities were affected with this kind of spinal rigidity, I proposed to designate it by the name *rhizomelic spondylosis*. . . .

After a careful review of the facts observed in his cases, he concludes:

It seems to me that it is permissible for clinicians to contrast deforming polyarthritis affecting the small joints of the extremities (acromelic deforming polyarthritis) with the ankylosing process that attacks primarily the spine and the joints at the roots or attachments of the extremities (rhizomelic spondylosis).

R. W. B.

MISCELLANY

ARMY-NAVY "E" AWARD TO SHARP AND DOHME, INCORPORATED

Sharp and Dohme, pioneers in the development of dried blood plasma, and producers in their laboratories in Philadelphia and nearby Glenolden not only of plasma but of many other disease-preventing, pain-relieving and life-saving medical supplies for the armed forces, were awarded the Army-Navy "E" for excellence in production on Wednesday, February 10. Since both pharmaceutical and biological laboratories received the award, two ceremonies were held. At each, the "E" pennant was presented by Brigadier General Hugh J. Morgan, chief consultant in medicine, Office of the Surgeon General, United States Army. The pennants were received on behalf of the company by Mr. J. S. Zinsser, the president.

NOTE

Dr. E. B. Astwood and Dr. E. W. Dempsey of the Harvard Medical School have been appointed managing editor and associate managing editor, respectively, of *Endocrinology*. They will have the collaboration of a newly established editorial board consisting of Drs. J. S. L. Browne, E. T. Engle, C. G. Hartman, E. C. Kendall, F. C. Koch, C. N. H. Long and H. B. van Dyke.

BOOK REVIEW

The Ophthalmic Formulary. Compiled by G. Griffin Lewis, M.D. 12°, cloth, 167 pp. Springfield, Illinois: Charles C Thomas, 1942. \$3.50.

In this volume the author has gathered 115 pages of ophthalmic prescriptions catalogued with reference to the eye diseases treated, and has added 27 pages of ophthalmic *materia medica*, 8 pages of index and 12 blank pages for notes.

Historically, just as the interest of the reader centers around the formulas set down in the *Ebers Papyrus* for treatment of the Egyptian ophthalmias, so also does the interest of the reader follow the empirical therapy practiced concurrently by each of the prescription authors of the present volume.

Practically, whether the reader of this volume be a general practitioner or an ophthalmologist, he already recognizes that therapy of today is departing from the field of the empirical and seeking a surer footing in the field of the etiologic and the chemical. Topical and empirical therapy in ophthalmology is nowadays deferring to more effective treatment: retinal detachment is referred at once to the experienced ophthalmic surgeon, and diabetic retinitis to the competent internist, and the exogenous and endogenous ophthalmic infections are discussed with and frequently treated by the chemotherapist.

The prospective buyer will purchase this volume to satisfy his curiosity about the therapeutic approach of his contemporary and departed colleagues, but he will not use it for his *vade mecum* in practice.

(Notices on page xii)

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SPORADIC INFECTIONS CAUSED BY *SALMONELLA SUIPESTIFER* AND *SALMONELLA ORANIENBURG**

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BOSTON

SPORADIC cases of *Salmonella suipestifer* infection continue to arouse interest because of their variable clinical manifestations. In the period of one year, 6 patients with this infection were observed at the Boston City Hospital. Two additional patients whom we originally believed to be infected with the organism were subsequently found to be infected with *S. oranienburg*, a closely related bacterium. This report presents the clinical, laboratory and bacteriologic findings of the 8 cases mentioned and a brief discussion in which the bacteriologic identification is emphasized.

CASE REPORTS

CASE 1. A C., a 63-year-old man, was readmitted on November 30, 1940, after having been discharged 5 months previously with a diagnosis of acute posterior coronary thrombosis, chronic bronchitis and arteriosclerotic heart disease with mild cardiac decompensation. Subsequently he was essentially well until 9 days before the present admission, when there was an onset of shaking chills followed by drenching sweats that recurred every evening. In addition there were marked irritability, intermittent mental confusion, anorexia, urinary frequency and progressive weakness.

Physical examination showed a chronically ill appearing male who was moderately confused. The chest was emphysematous. Moist rales were present at the base of each lung posteriorly. The heart appeared to be normal. The blood pressure was 110/60. The liver edge was felt 3 cm below the costal margin. The spleen was not palpable. The left leg was shortened, and the left femur was thickened along its entire shaft. The temperature was 102°F, the pulse 90, and the respirations 28. The hemoglobin was 90 per cent (Sihli). The red cell count was 4,480,000 and the white cell count 13,900 with 78 per cent polymorphonuclear leukocytes, 16 per cent lymphocytes and 6 per cent monocytes. The urine contained a heavy trace of albumin and many leukocytes. The blood Hinton reaction was negative. The plasma non-protein nitrogen was 48 mg per 100 cc.

The patient's course was one of gradual decline with periods of temporary improvement. Anorexia, nausea, weakness, delirium, chills and fever were the salient features. At no time was there any diarrhea or evidence of cardiac failure. During the first 10 days of hospitalization the temperature was persistently elevated, varying between 99° and 102°F. Thereafter there was a remittent type of fever with febrile episodes lasting for 2 to 5 days with intervening periods of subnormal temperature of 5 to 9 days duration. Occasionally rapid temperature rises were accompanied by shaking chills. The pulse varied between 70 and 110 and the respirations between 20 and 25. The hemoglobin fell gradually to 60 per cent. The white-cell count varied between 7500 and 15,000. Subsequent plasma non-protein nitrogen determinations showed no significant change from the initial level of 48 mg per 100 cc until the last week, when there was a rise to 199 mg. The urine, which had a maximum specific gravity of 1.030, consistently contained large amounts of albumin and variable numbers of leukocytes. The results of two lumbar punctures were negative. Two electrocardiograms showed no significant abnormality.

Röntgenograms of the chest were interpreted as emphysema, except for a film 2 days before death that showed a patchy infiltration at the base of the right lung. A film of the left femur showed changes consistent with osteitis fibrosa cystica within the shaft.

The patient received digitalis and toward the latter part of the illness parenteral fluids and small transfusions. From December 25 to January 2, 1941, he received a total of 46 gm of sulfadiazine without appreciable response, and from January 19 to 22 10 more. He became progressively weaker and died on January 29 approximately 10 weeks after the onset of the present illness. Terminally the clinical picture was that of uremia.

A blood culture taken on the day of admission was positive for *S. suipestifer*. Cultures taken on December 1, January 11, 15, 19, 24 and 29 were also positive for this organism, whereas those taken on January 6 and 16 were sterile. Neither of the sterile cultures was taken at a time when the patient was receiving chemotherapy. Between December 1 and January 29 seven urine cultures were positive for *S. suipestifer* and one taken on January 6 was sterile. Two stool cultures, a culture of sputum and a culture of prostatic secretion failed to yield this organism. On four occasions between December 8 and January 20 the patient's serum agglutinated his own organism and stock strains of *S. suipestifer* to a dilution of 1:640.

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Bacteriologic, Boston City Hospital.

Autopsy (performed 2 hours after death). The heart was moderately enlarged and weighed 610 gm. There was a slight dilatation of the apex of the heart, with softening of the muscle in this region and thickening of the overlying pericardium. On section the myocardium of the apex of the left ventricle was markedly thinned and on the underlying endocardial surface there was a large, firmly adherent, yellow thrombus which almost filled the lower half of the left ventricular chamber. The coronary arteries showed moderate sclerotic changes. The heart valves were normal. The right lower lobe of the lung showed a patchy pneumonic consolidation with multiple miliary abscesses. Elsewhere the lungs appeared normal. The spleen was slightly enlarged and at one pole there was a small yellow infarct. The liver was normal. The gastrointestinal tract was normal, except for a small duodenocolic fistula. The kidneys showed no significant abnormality other than a small infarct in the right kidney. The mucosal surface of the bladder was gray-black and roughened about the trigone. The left femur showed a fusiform dilatation of the shaft with destruction and replacement of bone by firm, gray tissue.

Histologically, the myocardium of the apex of the heart showed almost complete replacement by dense scar tissue. The attached mural thrombus showed evidence of organization in the deeper portion and superficially it was composed of fibrin, platelets and leukocytes. These changes indicated that the myocardial lesion was of at least several months' duration. The splenic infarct appeared recent in origin. The liver parenchyma was normal. The kidneys showed minimal changes that were consistent with slight benign nephrosclerosis. Sections of the left femur were consistent with localized osteitis fibrosa cystica.

A post-mortem culture of the heart's blood was sterile. A swab inserted in the endocardial thrombus was positive for *S. suispestifer*. Type 29 pneumococcus was the only organism cultured from the right lower lobe of the lung. Cultures of the spleen, of the liver, of bile aspirated from the hepatic duct and of the feces were negative for *S. suispestifer*. Gram-Weigert and MacCallum-Goodpasture stains of sections of myocardium, of the endocardial thrombus and of the splenic infarct showed no bacteria, so that it was impossible to prove satisfactorily that the endocardial thrombus was the focus responsible for the prolonged septicemia, in spite of the fact that the endocardial thrombus yielded *S. suispestifer*, while the heart's blood was sterile.

The pathological diagnoses were as follows: myocardial infarction, old, with mural thrombus; bronchopneumonia, with miliary abscesses, right lower lobe; slight benign nephrosclerosis; acute cystitis; small duodenocolic fistula; localized osteitis fibrosa cystica, left femur; surgical absence of gall bladder; and infarcts of spleen and right kidney.

CASE 2. C. M., a 48-year-old man, was admitted on March 19, 1941, because of dysuria and frequency of 2 months' duration.

The temperature was 98.6°F., the pulse 110, and the respirations 20. The heart and lungs were normal. The blood pressure was 160/100. Both kidneys were palpable, and there was moderate costovertebral tenderness on the right. The urine contained a heavy trace of albumin and many leukocytes. The hemoglobin was 90 per cent (Sahli), the red-cell count was 4,160,000, and the white-cell count was 12,200. The blood Hinton reaction was negative. The plasma nonprotein nitrogen level was 38 mg. per 100 cc. A retrograde pyelogram showed a single large stone in the dilated pelvis of the right kidney.

The day after admission the right kidney was removed. For the first 12 postoperative days, the patient was acutely ill, with the temperature varying between 100 and 103°F. thereafter the temperature was normal. On the 5th postoperative day, cough and pulmonary rales appeared. A roentgenogram was interpreted as indicating bronchopneumonia. At this time the patient was given 6 gm. of sulfathiazole daily for 1 week. He developed an anemia, with the hemoglobin falling to 60 per cent (Sahli), and the red-cell count to 3,000,000. Throughout the illness the white-cell count remained moderately elevated, varying between 10,000 and 20,000. Differential counts taken from the 2nd to 5th week of hospitalization showed from 60 to 80 per cent polymorphonuclear leukocytes and from 8 to 20 per cent monocytes, the rest of the cells being lymphocytes. The albumin disappeared from the urine within several days after operation; however, leukocytes were persistently present. At the time of operation, and on three subsequent occasions during the first 2 postoperative weeks, *S. suispestifer* was cultured from the wound. No preoperative urine cultures were obtained. Three blood cultures during the febrile postoperative period were sterile. Cultures of the throat, stools, urine and bile were negative for *S. suispestifer*. On the 7th postoperative day the patient's serum agglutinated his own organism and stock strains of *S. suispestifer* to a dilution of 1:640. He was discharged well on April 26.

The resected right kidney measured 18 by 9 by 5 cm. The renal cortex was narrowed, and there was a tremendous dilatation of the calyces and renal pelvis. A single stone, 3 cm. in diameter, was in the renal pelvis. Histologically the kidney showed changes consistent with hydronephrosis, pyelitis and slight chronic pyelonephritis. There were no abscesses in the renal parenchyma.

CASE 3. I. M., a 21-year-old, unmarried woman, was admitted on February 23, 1941, because of severe, crampy, right lower abdominal pain of 4 days' duration. This was accompanied by headache, feverishness, obstipation, nausea, anorexia and drowsiness. There were no chills, vomiting or diarrhea. There was no history of intercourse.

On examination the patient appeared moderately ill. The temperature was 101°F., and the pulse 120. The heart and lungs were normal. The liver and spleen could not be palpated. There was rebound tenderness in the right lower quadrant of the abdomen. The following day an exploratory laparotomy was performed. The appendix and the left fallopian tube were normal, whereas the right fallopian tube appeared markedly enlarged, thickened and reddened. There was a small amount of fibrinous exudate in the pelvis. A right salpingectomy and an appendectomy were performed. A culture of the pelvic exudate yielded *S. suispestifer*. Postoperatively the patient received 6 gm. of sulfanilamide daily for 3 days. The temperature and pulse fell slowly to normal by the 5th postoperative day. Convalescence was uneventful.

At the time of admission, the hemoglobin was 70 per cent (Sahli), the red-cell count 4,040,000, and the white-cell count 11,600. Subsequent white-cell counts varied between 7000 and 9000 with 60 to 70 per cent polymorphonuclear leukocytes and 4 to 8 monocytes, the rest of the cells being lymphocytes. The stools and urine were normal.

S. suispestifer was recovered from the pelvic exudate at operation on February 24. The same organism was recovered from cultures of the abdominal wound on three occasions during the next 3 weeks. Cultures of the throat, urine, stools, bile and cervix did not yield this

organism On March 2, the patient's serum failed to agglutinate her own organism or stock strains of *S. suis* agglutifer On five subsequent occasions between March 12 and 27, her serum agglutinated her own organism and stock strains of *S. suis* agglutifer to a dilution of 1:640

The resected fallopian tube was distended with thin sanguinopurulent material Histologically the changes were those of chronic salpingitis and pyosalpinx with a superimposed acute inflammatory reaction

CASE 4 E. P., a 4-year-old girl, was readmitted on January 8, 1941 Three weeks previously she had been discharged from this hospital, having made an uneventful convalescence from pertussis Except for a slight cough she was well until 1 week before the present admission, when there was an onset of fever and cough productive of blood tinged sputum

At the time of admission the patient appeared acutely ill The tonsils were moderately enlarged and injected The heart appeared to be normal Fine rales were heard throughout the entire chest, although there was no evidence of consolidation The remainder of the examination was negative The temperature was 105°F, the pulse 148 and the respirations 48 Laboratory studies showed the urine to be normal The hemoglobin was 92 per cent (Sahli), the red cell count 5,650,000, and the white cell count 8600, with 42 per cent polymorphonuclear leukocytes, 48 per cent lymphocytes and 10 per cent monocytes An x-ray film of the chest was interpreted as showing bronchopneumonia in the right hilar area The patient was given sulfathiazole, 0.5 gm every 4 hours for 48 hours On the 3rd hospital day, the temperature, pulse and respirations returned to normal Convalescence was uneventful On the 8th day, the hemoglobin was 67 per cent (Sahli) and the white cell count 12,400, with 62 per cent polymorphonuclear leukocytes and 38 per cent lymphocytes

A blood culture on January 9, the day after admission, was positive for *S. suis* agglutifer On January 14 and 20 the patient's serum failed to agglutinate her own organism and stock strains of *S. suis* agglutifer From a throat culture taken on January 15 at a time when the patient was afebrile, a Type 18 *A. pneumoniae* was recovered A urine culture on January 15 was sterile The patient was discharged on January 26 with a diagnosis of *S. suis* agglutifer bacteremia and bronchopneumonia

CASE 5 R. M., a 35-year-old man with a long history of alcoholism, was admitted on August 19, 1940 For 6 months he had had a chronic productive cough accompanied by anorexia, night sweats and loss of weight The day of admission he developed diarrhea and frequent shaking chills

On physical examination the patient appeared both acutely and chronically ill The temperature was 103°F, the pulse 90 and the respirations 20 The only abnormal finding in the chest was bronchial breathing at the right lung base posteriorly The liver was enlarged, extending 9 cm below the right costal margin The spleen was not palpable The patient had a severe macrocytic anemia There was no achlorhydria The white-cell count was 3400, with 62 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes and 6 per cent monocytes Subsequent counts varied between 6000 and 12,000 The urines and stools were normal Roentgenograms of the chest showed changes consistent with bronchiectasis of the right lower lobe

The patient remained in the hospital for 8 weeks The diarrhea subsided within 24 hours The temperature rose to 102°F on the 2nd day, returned to normal on the 3rd day, and for the next 10 days showed frequent rises to 99 or 100°F Thereafter the patient was afebrile The pulse varied between 80 and 110 The patient slowly gained weight and strength The macrocytic anemia responded to liver therapy The liver decreased in size Liver function tests on several occasions showed no impairment

A blood culture taken on the day of admission was positive for *S. suis* agglutifer Subsequent cultures of the blood, urine, stools, sputum and bile were negative for this organism The patient's serum on August 27 and September 11 failed to agglutinate his own organism and stock strains of *S. suis* agglutifer He was discharged on September 13 with a diagnosis of *S. suis* agglutifer septicemia chronic alcoholism, early cirrhosis of the liver, macrocytic anemia of undetermined etiology, malnutrition and bronchiectasis

CASE 6 W. C., a 44-year-old man, was admitted on October 23, 1940 There was a history of chronic alcoholism For the past 4 months there had been an intermittent productive cough Two weeks before admission, the patient had several shaking chills which were followed by sweats Two days later, he experienced a pleuritic type of pain in the region of the right lower chest and his cough became productive of brownish sputum The present illness was attended by malaise and dull epigastric pain

Physical examination revealed a well developed, poorly nourished man who appeared moderately ill The tongue, which showed moderate atrophy of the papillae, exhibited a coarse tremor There was slightly diminished resonance over the left chest anteriorly and posteriorly and occasional rales were heard in these areas The heart appeared to be normal The blood pressure was 154/90 The liver edge was felt at the right costal margin The spleen was not palpable Physical examination was otherwise negative

The temperature was 100.8°F, the pulse 112, and the respirations 28 The hemoglobin was 89 per cent (Sahli) The red cell count was 3,850,000 The white-cell count was 4600, with 54 per cent polymorphonuclear leukocytes, 44 per cent lymphocytes and 2 per cent monocytes Subsequent counts varied between 4800 and 5200 Repeated examinations of the urine and stools were normal The blood Hinton reaction was negative On repeated examinations of the sputum, no tubercle bacilli were present A roentgenogram showed the lung fields to be clear

The patient received supportive treatment supplemented by vitamin therapy The temperature remained elevated for the 1st week of hospitalization, varying between 99 and 101°F, and thereafter was normal The pulse varied between 70 and 90 On the 4th hospital day, the patient became jaundiced, with an icteric index of 25 Four days later the jaundice had subsided At the onset of the jaundice the liver edge was palpable 4 cm below the costal margin Recovery was gradual

A blood culture on October 29, 6 days after admission, yielded *S. suis* agglutifer Subsequent blood cultures taken on October 31 and November 1 and 2 were sterile On October 28, a Type 14 *A. pneumoniae* was recovered from the sputum A culture of urine on November 2 and stool cultures on November 2 and 4 were negative for *S. suis* agglutifer The patient's serum on November 2, 8 and 19 agglutinated his own organism and stock strains of *S. suis* agglutifer to a dilution of 1:640

The patient was discharged on November 24 with a diagnosis of chronic alcoholism, acute infectious hepatitis, early cirrhosis of the liver, deficiency of vitamin B complex and *S. suispestifer* bacteremia.

Certain findings in this small series of 6 cases of *S. suispestifer* infection deserve comment. Only 1 case occurred in a child, the remaining 5 in adults. In no case was the source of infection determined.

Harvey¹ divided 71 cases of sporadic *S. suispestifer* infection into clinical groups. Most numerous were the typhoidlike infections, in which there were no localizing signs. Fever, anorexia, vomiting, headache and diarrhea were the commonest symptoms. The pulse was usually rapid. Mild bronchitis was frequent in older patients. A second large group of patients had pulmonary involvement, as evidenced by bronchopneumonia, occasional lobar pneumonia, pleurisy with effusion and empyema. A third group included suppurative bone and joint lesions due to this organism. A fourth group was comprised of infections complicating surgical procedures. In additional groups were placed the more unusual complications, such as involvement of the nervous system, endocarditis and urinary-tract infection.

Two of our 6 cases of *S. suispestifer* infection fall into the group with typhoidlike symptoms. In Case 1, however, the anatomical findings suggested that an endocardial thrombus might have been a focus of infection, although this could not be established with certainty. In this respect, the case was more analogous to a *S. suispestifer* endocarditis, which has occasionally been observed.²⁻⁵

In 5 cases there was clinical or roentgenologic evidence of pulmonary involvement. In 2 cases (Cases 4 and 6) the pulmonary complications were a prominent feature in the present illness, while in 2 others (Cases 1 and 2) they appeared to be incidental. In Case 5, the pre-existing bronchiectasis seemed unrelated to the present illness. In all 6 cases, cultures of the sputum or throat failed to yield *S. suispestifer*. In Cases 4 and 6, pneumococci recovered from the sputum and from a throat culture may have been responsible for the pulmonary infection. In Case 1, at autopsy there was a bronchopneumonia. Cultures from the affected lobe yielded only Type 29 pneumococcus. In only 6 of the 24 cases of *S. suispestifer* infection with pulmonary complications described by Harvey¹ was there bacteriologic proof that this organism was responsible for the pulmonary changes. Kuttner and Zepp⁶ describe the case of a two-year-old child who had *S. suispestifer* bacteremia. At autopsy this organism was recovered from the heart's blood, whereas a Type 3 pneumococcus and the influenza bacillus were the only organisms

present in cultures of the lungs. These observations suggest that pulmonary involvement occurring during the course of this infection may be caused by other bacteria that may be regarded as accompanying or secondary infections.

Cases of *S. suispestifer* infection in which the urinary-tract infection has a prominent role in the clinical symptoms are unusual.¹ In Case 2, a large single renal calculus causing obstruction was associated with *S. suispestifer* infection in the involved kidney.

Acute abdominal conditions resulting from *S. suispestifer* infection have been relatively frequent. Kuttner and Zepp⁷ described a case of fibrinous peritonitis due to this organism. Walker, Weiss and Nye⁸ described a case of *S. suispestifer* bacteremia complicated by a large splenic abscess. From a case with chronic cholecystitis, they cultured from the gall bladder an organism which although not fully identified was presumed to be *S. suispestifer*. In Case 3 of our series, there was a unilateral salpingitis with a localized fibrinous peritonitis from which *S. suispestifer* was cultured. Herring and Nicholson⁹ described a case with bilateral acute salpingitis and pelvic peritonitis due to this organism. TenBroeck and his co-workers¹⁰ described a *S. suispestifer* infection in association with an induced abortion and subsequent sepsis. Boller¹¹ observed a *S. suispestifer* infection associated with postpartum sepsis. In a case described by Gray,¹² *S. suispestifer* septicemia was associated with multiple infected uterine myomas.

Certain other clinical findings were of interest in our series. Fever was present in 5 cases at the time of admission and developed in the other post-operatively. Two patients had chills. Diarrhea occurred only once. Relative bradycardia occurred once. There was enlargement of the liver in 3 cases; in 2, however, there was a history of chronic alcoholism. Jaundice occurred in 1 case and was of brief duration. Splenomegaly was not observed. Chemotherapy, which was employed in 4 cases, did not seem to have a beneficial effect in any. Four patients were debilitated prior to the onset of the illness, either by previous illness or chronic alcoholism.

The blood findings deserve mention. A moderate anemia was present or developed during the course of the illness in 4 cases; in several of them, however, chemotherapy may have been a factor in its production. In 3 cases the initial white-cell count was low or normal, whereas in 3 it was elevated. In 2 cases the urine contained albumin and leukocytes.

In 4 of the 5 cases in which blood cultures were made, the organism was recovered. Urine cultures were positive in only 1 case. Stool cultures were

negative in every case. Prostatic secretion in 1 case and culture of the cervix in 1 did not yield this organism. Sputum or throat cultures were made in every case, but *S. supestifer* was not recovered. Cultures of the bile were made in 3 cases and gave negative results. Cultures of the wounds in the 2 cases with surgical complications

flagellar antigen *c* *S. paratyphi* C (*Bacterium paratyphosum* C, eastern European type of *S. supestifer*, Hirschfeld type) is likewise diphasic and may occur in the group phase with flagellar components 1, 4 and 5 or in the type specific phase with the flagellar antigen *c*. In addition, there are several allied types of *S. supestifer* that differ

TABLE 1 Fermentation Reactions

ORGANISM	SUGAR FERMENTATIONS*										H ₂ S PRODUCTION
	DEXTROSE	LACTOSE	SUCROSE	XYLOSE	ARABINOSE	RHAMNOSE	INOSITE	MANNITE	DULCITE	TRIALOSE	
<i>S. cholerae</i> <i>suis</i> var. <i>kunzendorf</i>	AG	-	-	AG	-	AG	-	AG	↑	-	+
<i>S. cholerae</i> <i>suis</i>	AG	-	-	AG	-	AG	-	AG	-	-	+
<i>S. paratyphi</i> C	AG	-	-	AG	AG	AG	-	AG	AG	AG	+
<i>S. oranienburg</i>	AG	-	-	AG	AG	AG	-	AG	AG	AG	+
Case 1	AG	-	-	AG	-	AG	-	AG	↑	-	+
Case 2	AG	-	-	AG	-	AG	-	AG	-	-	+
Case 3	AG	-	-	AG	-	AG	-	AG	↑	-	+
Case 4	AG	-	-	AG	-	AG	-	AG	-	-	+
Case 5	AG	-	-	AG	-	AG	-	AG	↑	-	+
Case 6	AG	-	-	AG	-	AG	-	AG	-	-	+
Case 7	AG	-	-	AG	AG	AG	-	AG	AG	AG	+
Case 8	AG	-	-	AG	AG	AG	-	AG	AG	AG	+

* AG = fermentat on with the format on of ac d and gas

= no fermentat on

↑Delayed fermentat ion (5 to 14 days)

gave repeatedly positive results. In 4 cases, the patients' serums agglutinated their organisms. In 3, this was manifest during the third or fourth week of illness and may have appeared earlier. In 1 case, the duration of the illness could not be ascertained. In 2 cases, the patients' serums did not agglutinate their organisms by the fourth week and no subsequent studies were made.

S. supestifer is a gram negative motile bacillus that can be separated from other members of the *Salmonella* group by its selective fermentation reactions and by agglutinations with specific anti-serums. It belongs in Group C of the Kauffmann-White classification¹³ of the typhoid paratyphoid organisms. The organisms in Group C have in common at least one of the two somatic antigens V and VII. The term "*Salmonella supestifer*" includes several organisms that have both the somatic antigens VI and VII but differ slightly in their flagellar antigenic components and in their selective fermentation reactions (Table 1). *S. cholerae suis*, var. *kunzendorf* (monophasic, western European type of *S. supestifer*, Group II of Andrews¹⁴) is a monophasic organism with group flagellar antigens 1, 3, 4 and 5, which are shared by certain other members of the *Salmonella* group. *S. cholerae suis* (diphasic, American strain of *S. supestifer*, Group I of Andrews) exists in two phases. In one phase, this organism has the group flagellar antigens 1, 3, 4 and 5, which are identical with those of the monophasic organism (*S. cholerae suis*, var. *kunzendorf*), whereas in the other phase this organism has only the type specific

slightly in their selective fermentation reaction but have the same antigenic structure.

According to Kauffmann,¹³ the majority of diphasic *Salmonella* organisms tend to occur predominantly in the specific phase when freshly isolated. Such an organism gives rise to substrains that occur in the specific phase and the group phase.^{13, 14} It is apparent that organisms of the diphasic strain can occur predominantly in the non-specific phase in a given culture. In this event, *S. cholerae suis*, a diphasic organism, would be antigenically indistinct from *S. cholerae suis*, var. *kunzendorf*, a monophasic type. It was formerly assumed that monophasic types never give rise to substrains of the diphasic type. This view has been refuted by Bruner and Edwards,^{15, 16} who were able to obtain diphasic strains from monophasic strains by special culture technique. Under ordinary cultural conditions, however, this change did not occur.

The six strains of *S. supestifer* isolated from our cases belong to the type *S. cholerae suis*, var. *kunzendorf*, a monophasic organism. In America, infections in man from both the diphasic type (*S. cholerae suis*) and the monophasic type (*S. cholerae suis*, var. *kunzendorf*) have been observed. In recent years, however, the monophasic type has been found more frequently.^{4, 6, 10} To our knowledge, the Hirschfeld strain (*S. paratyphi* C) has not been found in this country.

From selective fermentation reactions, our six strains belonged to the monophasic type. For absolute identification, agglutinin absorption studies

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Harvey¹ divided 71 cases of sporadic *S. suispestifer* infection into clinical groups. Most numerous were the typhoidlike infections, in which there were no localizing signs. Fever, anorexia, vomiting, headache and diarrhea were the commonest symptoms. The pulse was usually rapid. Mild bronchitis was frequent in older patients. A second large group of patients had pulmonary involvement, as evidenced by bronchopneumonia, occasional lobar pneumonia, pleurisy with effusion and empyema. A third group included suppurative bone and joint lesions due to this organism. A fourth group was comprised of infections complicating surgical procedures. In additional groups were placed the more unusual complications, such as involvement of the nervous system, endocarditis and urinary-tract infection.

Two of our 6 cases of *S. suispestifer* infection fall into the group with typhoidlike symptoms. In Case 1, however, the anatomical findings suggested that an endocardial thrombus might have been a focus of infection, although this could not be established with certainty. In this respect, the case was more analogous to a *S. suispestifer* endocarditis, which has occasionally been observed.²⁻⁵

In 5 cases there was clinical or roentgenologic evidence of pulmonary involvement. In 2 cases (Cases 4 and 6) the pulmonary complications were a prominent feature in the present illness, while in 2 others (Cases 1 and 2) they appeared to be incidental. In Case 5, the pre-existing bronchiectasis seemed unrelated to the present illness. In all 6 cases, cultures of the sputum or throat failed to yield *S. suispestifer*. In Cases 4 and 6, pneumococci recovered from the sputum and from a throat culture may have been responsible for the pulmonary infection. In Case 1, at autopsy there was a bronchopneumonia. Cultures from the affected lobe yielded only Type 29 pneumococcus. In only 6 of the 24 cases of *S. suispestifer* infection with pulmonary complications described by Harvey¹ was there bacteriologic proof that this organism was responsible for the pulmonary changes. Kuttner and Zepp⁶ describe the case of a two-year-old child who had *S. suispestifer* bacteremia. At autopsy this organism was recovered from the heart's blood, whereas a Type 3 pneumococcus and the influenza bacillus were the only organisms

present in cultures of the lungs. These observations suggest that pulmonary involvement occurring during the course of this infection may be caused by other bacteria that may be regarded as accompanying or secondary infections.

Cases of *S. suispestifer* infection in which the urinary-tract infection has a prominent role in the clinical symptoms are unusual.¹ In Case 2, a large single renal calculus causing obstruction was associated with *S. suispestifer* infection in the involved kidney.

Acute abdominal conditions resulting from *S. suispestifer* infection have been relatively frequent. Kuttner and Zepp⁷ described a case of fibrinous peritonitis due to this organism. Walker, Weiss and Nye⁸ described a case of *S. suispestifer* bacteremia complicated by a large splenic abscess. From a case with chronic cholecystitis, they cultured from the gall bladder an organism which although not fully identified was presumed to be *S. suispestifer*. In Case 3 of our series, there was a unilateral salpingitis with a localized fibrinous peritonitis from which *S. suispestifer* was cultured. Herring and Nicholson⁹ described a case with bilateral acute salpingitis and pelvic peritonitis due to this organism. TenBroeck and his co-workers¹⁰ described a *S. suispestifer* infection in association with an induced abortion and subsequent sepsis. Boller¹¹ observed a *S. suispestifer* infection associated with postpartum sepsis. In a case described by Gray,¹² *S. suispestifer* septicemia was associated with multiple infected uterine myomas.

Certain other clinical findings were of interest in our series. Fever was present in 5 cases at the time of admission and developed in the other post-operatively. Two patients had chills. Diarrhea occurred only once. Relative bradycardia occurred once. There was enlargement of the liver in 3 cases; in 2, however, there was a history of chronic alcoholism. Jaundice occurred in 1 case and was of brief duration. Splenomegaly was not observed. Chemotherapy, which was employed in 4 cases, did not seem to have a beneficial effect in any. Four patients were debilitated prior to the onset of the illness, either by previous illness or chronic alcoholism.

The blood findings deserve mention. A moderate anemia was present or developed during the course of the illness in 4 cases; in several of them, however, chemotherapy may have been a factor in its production. In 3 cases the initial white-cell count was low or normal, whereas in 3 it was elevated. In 2 cases the urine contained albumin and leukocytes.

In 4 of the 5 cases in which blood cultures were made, the organism was recovered. Urine cultures were positive in only 1 case. Stool cultures were

16,400, with 90 per cent polymorphonuclear leukocytes and 10 per cent lymphocytes. Subsequent counts varied between 7800 and 10,000. The urine contained a heavy trace of albumin and many leukocytes in the sediment. A Type 33 pneumococcus was cultured from the sputum. A roentgenogram showed consolidation of the right middle lobe of the lung.

The patient was given 0.5 gm of sulfathiazole every 4 hours for 3 days. The temperature fell to normal on the 2nd day and then rose again, reaching 104°F on the 4th day. On the 5th day it returned to normal, where it remained. The physical signs of pneumonia and diarrhea disappeared by the 7th day. The diarrhea recurred on the 10th day and continued for 5 days. The urine consistently showed heavy traces of albumin, although there were no leukocytes in the urinary sediment after the 4th day. The plasma nonprotein nitrogen determination on the 7th day was 46 mg per 100 cc.

A blood culture taken the day after admission yielded *S. oranienburg*. A culture on April 14 was sterile. Urine cultures on April 15 and 19 and May 5 did not yield this organism. *S. oranienburg* was recovered from stool specimens on April 10 and 15, but not from stool cultures on May 7 and 8. A throat culture on April 15 was negative for this organism. On April 15 and May 27 the patient's serum agglutinated his organism to a dilution of 1:160.

S. oranienburg is a rare pathogen. Kauffmann¹⁸ isolated it from several healthy individuals and from the stools of 3 children with diarrhea. Rimpau and Steinert¹⁹ isolated it repeatedly from the stools of a healthy carrier, whose serum did not agglutinate the organism. They also isolated this organism from the stool of a woman with acute gastroenteritis. This patient's serum was found to agglutinate her organism to a dilution of 1:200 when tested eight days after onset of illness.

S. oranienburg is a monophasic organism which has the somatic antigens VI and VII and the type specific flagellar antigens *m* and *t*. As noted in Table 1, the selective fermentation reactions of this organism are identical with those of *S. paratyphi C*. If, however, we had carried out fermentation tests with Stern's glycerol medium and Bitter's rhamnose medium,¹⁸ it would have been possible to make a differentiation, since *S. oranienburg* gives positive fermentation reactions on these two mediums, whereas *S. paratyphi C* yields negative reactions. With stock *S. supestifer* serum, *S. oranienburg* gives a somatic (finely granular) type

of agglutination. This is in accord with their common somatic antigens. The diphasic *S. supestifer* (*S. cholerae suus*) serum absorbed with the monophasic strain (*S. cholerae suus*, var. *kunzendorf*) failed to agglutinate the two *S. oranienburg* strains. This is to be expected, since the two organisms have distinct flagellar antigens. When injected subcutaneously and intraperitoneally into mice, the two *S. oranienburg* strains proved lethal.

SUMMARY

Six sporadic human cases of infection with *S. supestifer* are described. Clinically these cases showed great variation. The bacteriologic identification of this organism and its separation into types are discussed. Two cases of *S. oranienburg* infection are described, and the close bacteriologic similarity of this organism with *S. supestifer* is considered.

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RHEUMATOID ARTHRITIS AS A CAUSE OF INCREASED CEREBROSPINAL-FLUID PROTEIN*

A Study of One Hundred and One Patients

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THE neurologic manifestations of rheumatoid arthritis are numerous, extremely variable and at times so striking as to simulate disease of the central or peripheral nervous system. They comprise evidence of increased vasomotor activity, such as cold, clammy, cyanotic extremities, vasospasm, tachycardia and visual-field defects; sensory phenomena, including paresthesia, changes in sensory perception and referred radiating pains with radicular or segmental distribution; abnormalities of the motor system marked by muscular weakness, atrophy and hyperirritability, leading to tremor, twitchings, cramps and changes in the tendon reflexes; and possibly trophic changes of the skin, hair and nails. One or more such clinical features of the disease have been observed in 66 per cent of 293 unselected consecutive patients with rheumatoid arthritis. An analysis of these findings and the results of detailed neuropathological studies will be the subject of a future report.¹

The present investigation, concerning the cerebrospinal-fluid findings in rheumatoid arthritis, was begun in 1935. In the meantime, Graber-Duvernay and Gerbay,² employing an inexact method for the determination of protein, reported an elevated cerebrospinal-fluid protein in 8 of 15 patients with moderate to severe rheumatoid arthritis, of whom only 1 had spondylitis. A little later, Marron,³ using a tyrosine equivalent method for protein analysis, noted cerebrospinal-fluid proteins varying from 31 to 60 mg. per 100 cc. in 6 cases of arthritis of the spine, unspecified as to type. Except for these two papers, a search of the literature has failed to reveal any reference to the subject.

MATERIALS AND METHODS

The cerebrospinal fluids examined during the course of this study were obtained from 101 patients with rheumatoid arthritis, of whom 59 suffered from peripheral-joint disease alone and 42

from spondylitis, with or without peripheral-joint involvement. All were under our personal observation, many being in the group of 293 cases previously referred to. The diagnosis of spondylitis was based on stiffness, pain, tenderness, limitation of motion and deformity of the spine. There was frequently a history of sciatica or intercostal, segmental or pleuritic pain. Straight leg-raising was usually limited and often associated with some restriction of the motions of either the hips or shoulders or both. As a rule the chest expansion and vital capacity were markedly reduced. Increased knee and ankle jerks were commonly found, and an absent Achilles-tendon reflex (at the time the sciatica was present), meralgia paraesthetica and other neurologic abnormalities were demonstrable in some cases. Roentgenologic evidence of disease of the sacroiliac or spinal articulations was present in all but 1 of the spondylitis group, the exception being an early case with typical findings of rheumatoid spondylitis. All these patients had elevated sedimentation rates.

Since it was soon apparent that cerebrospinal fluid abnormalities were encountered more frequently in the patients with spondylitis, we included more patients with this type of rheumatoid

TABLE 1. Distribution of Patients according to Age and Sex.

Age	WITHOUT SPONDYLITIS			WITH SPONDYLITIS		
	MALES	FEMALES	TOTAL	MALES	FEMALES	TOTAL
Under 20 yr.	5	6	11	5	0	5
20 to 39 yr.	5	20	25	23	5	28
40 to 59 yr.	5	15	20	7	2	9
60 yr. and over	2	1	3	0	0	0
Totals	17	42	59	35	7	42

arthritis. As a result, the age and sex distribution of the cases studied and the ratio of one group to the other are not the same as they would be in an unselected consecutive series (Table 1). However, it will be seen from Table 2 that the distribution by duration and severity of disease is more nearly comparable to what one might expect to find in an unselected group of cases.

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Cerebrospinal-fluid analyses* were repeated in 11 cases (7 with and 4 without spondylitis), with intervals ranging from two weeks to three years. The following chemical methods were used: sugar, Folin⁴; chloride, Wilson and Ball⁵;

TABLE 2. *Distribution of Patients according to Duration and Severity of Disease.*

	DURATION			SEVERITY		
	UNDER 1 YR.	1-5 YR.	OVER 5 YR.	MILD	MODERATE	SEVERE
Without spondylitis	14	29	16	14	25	20
With spondylitis	5	18	19	5	19	18
Totals	19	47	35	19	44	38

protein, Ayer, Dailey and Fremont-Smith⁶; colloidal-gold curve, Lange.⁷ We have considered the following values as being characteristic of normal cerebrospinal fluid⁸: initial pressure, 70 to 180 mm. of water (pressures of 180 to 200 mm. and greater than 200 mm. are thought to be questionably abnormal and definitely increased respectively); leukocytes, 0 to 5 cells per cu. mm.; sugar, 50 to 100 mg. per 100 cc.; chlorides, 695 to 762 mg. per 100 cc.; protein, lumbar fluid, 15 to 45 mg. per 100 cc., and cistern fluid, 15 to 25 mg. per 100 cc.; colloidal-gold curve, no change greater than 2 in each tube.

RESULTS

The initial pressure, measured in 93 cases, was normal in all but 7. In 5 it was questionably abnormal (in 1 case 195 mm. and in 4 cases 200 mm. of water), and in 2 it was definitely high (210 and 250 mm. of water). In only 1 of the latter was the protein content increased. In the absence of

in the other 3 cases (46.0, 48.0 and 48.5 mg. per 100 cc.) are not significant. The chloride determinations in only 3 of 34 cases were lower than normal (693, 690 and 670 mg. per 100 cc.). Minor reductions of this type, particularly when not accompanied by other changes, are of no diagnostic importance.⁸ Similarly, we did not regard as significant total protein values of 12 to 14 mg. per 100 cc.⁸ observed in fluids from 5 patients in the group with peripheral-joint involvement alone, 4 of whom were under eighteen years of age.

The number of patients having increased cerebrospinal-fluid proteins and abnormal colloidal-gold curves is shown in Table 3. It will be noted that the percentage of fluids showing an increased protein content was significantly higher in the spondylitis group than in the group with

TABLE 4. *Increased Cerebrospinal Fluid Protein Contents and the Colloidal Gold Reactions in Patients without Spondylitis.*

DATE	NAME OF PATIENT	SEX	AGE	PROTEIN CONTENT mg / 100 cc	GOLD SOL CURVE	TYPE OF FLUID
4/13/35	J R W	M	35	46	0000000000	Lumbar
4/8/36	B D	M	54	47	0012321100	Lumbar
11/10/35	W S D	M	64	55	0000121100	Lumbar
3/7/36				25	0000000000	Lumbar
2 1/2/35	J Mcl	M	49	66	0001233310	Lumbar
1 1/2/35				70		Lumbar
				51		Dorsal
				40		Cistern

peripheral involvement alone, and that only a small proportion of the fluids gave an abnormal colloidal-gold curve.

The increased cerebrospinal-fluid protein contents observed in the individual patients without

TABLE 3. *Incidence of Increased Cerebrospinal-Fluid Protein Contents and Abnormal Colloidal-Gold Reactions in Patients without and with Spondylitis*

PATIENTS	WITHOUT SPONDYLITIS				WITH SPONDYLITIS				PERCENTAGE DIFFERENCE
	MALES		FEMALES	TOTAL	MALES		FEMALES	TOTAL	
	No	%	No		%				
All examined	17	42	59		35	7	42		
Those with a high total protein	4	0	4	6.8	11	1	12	28.6	19.8 (±7.4)
Those with an abnormal colloidal gold reaction	2	3	5	8.5	6	0	6	15.0	6.5 (±6.4)

other abnormalities, these slightly increased initial pressures probably represent incomplete relaxation of the patient. Pleocytosis was present in 3 cases, but all the fluids were contaminated with blood in sufficient quantity to explain the increase in white cells. In 41 of 44 cases the sugar determinations were normal. The slight reductions observed

spondylitis are listed separately in Table 4. Fluids from 3 other patients in this group exhibited an increased colloidal-gold reaction but were otherwise normal; these curves are shown in Table 5.

Thus it will be seen that only 9 of the 59 patients with rheumatoid arthritis involving the peripheral joints alone had spinal-fluid alterations, 4 having increased proteins, 2 (J. Mcl. and B. D.) with associated abnormal gold-sol curves, and 3 having only abnormalities of the gold-sol curve

*The cerebrospinal fluid determinations were carried out in the Spinal Fluid Laboratory of the Massachusetts General Hospital by Miss Eulizia Grebeniowska and Mrs Charles McCann, to whom we are indebted for their services.

The latter changes usually occurred in the first and middle zones. Lumbar punctures were repeated in 4 cases from this group. In 2, both fluids were normal. In patient J. McL., re-examination confirmed the finding of a previous high protein,

TABLE 5. *Abnormal Colloidal-Gold Reactions in Cerebrospinal Fluids without Increased Protein Content in Patients without Spondylitis.*

NAME OF PATIENT	SEX	AGE yr.	PROTEIN CONTENT mg / 100 cc.	GOLD SOL CURVE
L S	F	34	31	1123210000
S K	F	36	30	1233221000
R R	F	35	32	555552100

but in patient W. S. D. the second fluid was normal. He entered the hospital complaining of acute rheumatoid arthritis and frequent nocturnal erections. Although the protein was elevated at that time, there was no evidence of neurologic disease. A urethral stricture was present and was thought.

TABLE 6. *Increased Cerebrospinal-Fluid Protein Contents and the Colloidal-Gold Reactions in Patients with Spondylitis.*

DATE	NAME OF PATIENT	SEX	AGE	PROTEIN CONTENT mg / 100 cc	GOLD SOL CURVE	TYPE OF FLUID
6/14/39	F M.	M	34	47	0001210000	Lumbar
6/13/41	E A	M	39	48	0011110000	Lumbar
5/9/40	H E	M	15	51	0012221000	Lumbar
5/16/40				25	0001111000	Lumbar
7/25/40				65	0122332100	Lumbar
6/25/40	A McK	M	23	53	0001110000	Lumbar
1/30/41				55	0011100000	Lumbar
1/27/41	A L	M	53	58	0122210000	Lumbar
2/1/40	J dP	M	27	60	5555533100	Lumbar
5/23/40				58	5555533110	Lumbar
11/29/40				51	5555533100	Lumbar
1/26/39	R G	M	21	60	0011221000	Lumbar
1/26/39				44		Lumbar
5/8/39				41	0011221000	Lumbar
3/28/41	H O D	M	44	60		Lumbar
5/31/40	W D	M	33	80	0012211000	Lumbar
6/18/41	Q M	F	48	85		Lumbar
4/17/41	W N B	M	26	103	0001222100	Lumbar
12/31/37	M L V	M	41	105	0000122100	Lumbar
1/25/38				121	0001221000	Lumbar
1/25/38				31		Cistern

to explain the genital symptoms. Re-examination was made three years later, at a time when the arthritis was quiescent but the erections continued.

Increased cerebrospinal-fluid protein was found in 12 of the 42 patients having spondylitis. The values are given in Table 6. Two of these 12 patients (H. E. and J. dP.) and 4 others without associated high protein had abnormal gold-sol curves. The latter are shown in Table 7.

Of the 7 patients in the spondylitis group in whom the spinal fluid was examined on more than

one occasion, 3 were consistently abnormal (high protein, with or without abnormal gold-sol curves), 2 were consistently normal except for a questionably abnormal initial pressure in 1, and 2 (R. G. and H. E.) showed a high protein content or an abnormal gold-sol curve on some occasions and were normal on others. (See Table 6.)

Thus it will be seen that 23 of the 101 patients had cerebrospinal-fluid alterations, 16 with increased protein contents, with or without accompanying increased colloidal-gold reactivity, and 7

TABLE 7. *Abnormal Colloidal-Gold Reactions in Cerebrospinal Fluids without Increased Protein Content in Patients with Spondylitis.*

NAME OF PATIENT	SEX	AGE yr.	PROTEIN CONTENT mg / 100 cc	GOLD SOL CURVE
R. F.	M	32	20	5555211000
J. N.	M	36	29	4333211000
L S	M	35	29	1233310000
H W.	M	58	40	1122321000

with abnormal colloidal-gold curves only. As previously noted, 12 of the 16 patients with elevated proteins had spondylitis. In view of this finding, it is of considerable interest that 3 of the 4 patients (all males) in the group with peripheral-joint involvement showing elevated proteins had clinical symptoms suggestive of spondylitis at the time of the lumbar puncture. A definite diagnosis of spondylitis was not justified at the time, but one of the patients (J. R. W.) developed roentgenologic changes in the sacroiliac articulations at a later date. The fact that 15 of the 16 patients with increased proteins had either spondylitis (12 cases) or symptoms indicative of spinal involvement (3 cases) strongly suggests a relation between an elevation of the cerebrospinal-fluid protein and the presence of rheumatoid arthritis in the spinal and sacroiliac articulations. In the 2 patients with high proteins in whom cistern punctures were also performed (J. McL. of the peripheral group and M. L. V. of the spondylitic group), the fluid also showed an elevation of protein (40 and 31 mg. per 100 cc., respectively), as did fluid taken simultaneously from the dorsal region in the case of J. McL.

No significant relation could be established between the level of the spinal-fluid protein and the age or sex of the patients with spinal involvement (except that spondylitis occurs predominantly in males), the duration or total severity of the disease or the sedimentation rate. Table 8 shows that severe pain or sciatica or both were much more frequent in the high-protein group, which suggests that these patients were suffering from more active disease.

DISCUSSION

It is generally agreed that abnormal gold sol curves are related to the cerebrospinal fluid albumin globulin ratio, the globulin fraction be

TABLE 8 Incidence of Severe Pain and Sciatica in Spondylitis Patients with and without Increased Cerebrospinal Fluid Protein Contents

SYMPTOMS	PROTEIN CONTENT		PERCENTAGE DIFFERENCE	
	NO	%	NO	%
Mild or moderate pain without sciatica	23	86.7	3	25.0
Severe pain or sciatica or both	7	23.3	9	75.0
Totals	30		12	

ing more active in causing the reaction⁸⁻¹¹ More recently, Kabat et al.,¹¹ employing the Tiselius electrophoresis apparatus, showed that in certain

in the globulin (the latter resulting in abnormal gold sol curves) are due chiefly to an increased permeability of the spinal-cord membranes as a result of their proximity to acutely inflamed articular tissues. The findings in Tables 8 and 9 are consistent with such a premise. That the increased permeability is greatest in the lumbar region is suggested by the diminishing protein content of fluids taken simultaneously from higher levels (the dorsal region and the cisterna magna). In these cases, the protein increase was not uniformly distributed through the subarachnoid space, as is the case in a metabolic disorder, such as myxedema.⁸

Diagnostic Implications

The diagnosis of spondylitis, especially in early cases, may at times be extremely difficult. This is particularly true of patients having an increased cerebrospinal fluid protein, complaining of back pain with sciatic radiation (increased by coughing

TABLE 9 Relation between Abnormal Cerebrospinal Fluid Protein Contents and Gold-Sol Curves and Serum Globulin

TYPE OF INVOLVEMENT	NO OF CASES	SERUM			CEREBROSPINAL FLUID	
		INCREASED PROTEIN	INCREASED GLOBULIN	INCREASED PROTEIN	GLOBULIN PRESENT	ABNORMAL GOLD-SOL CURVE
Peripheral	4	0	0	0	No determination	0
	7	4	7	0	No determination	1
Spondylitic	3	0	0	0	No determination	0
	4	3	4	3	3	3

diseases all the colloidal gold reactivity was found in the gamma globulin fraction and none in the albumin fraction. They stated, "Although the colloidal gold reacting material is found in the gamma fraction, it may differ from the normal gamma component of spinal fluid, since other fluids which contain equally large amounts of gamma globulin yield normal colloidal gold curves." They were also able to demonstrate that cerebrospinal fluid proteins show a similar pattern to that of the serum proteins. Since it is known that the serum albumin globulin ratio may be reversed in patients with rheumatoid arthritis, with or without elevation of the serum protein,¹²⁻¹⁴ it seemed logical to suspect that the spinal fluid protein and colloidal gold curve abnormalities were a reflection of alterations in the serum proteins. The latter were determined in too small a number of cases to draw any definite conclusions. The data suggest, however, as shown in Table 9, that, in cases with spondylitis, abnormal gold sol curves are related to elevation of the serum globulin. It is possible that these abnormalities are related, in part, to the types or concentrations of globulin in such cases.¹¹ However, it is more likely that changes in the total cerebrospinal fluid protein or

and sneezing) and exhibiting flattening of the lumbar curve, diminution of motion of the lumbar spine and of straight leg raising, and atrophy and weakness of the muscles of the thighs and legs. The neurologic examination is, as a rule, negative except for hyperreflexia, although meralgia paraesthetica and an absent Achilles tendon reflex are rarely observed. In such cases the diagnostic possibilities include ruptured intervertebral disk, intraspinal neoplasm, metastatic malignant disease, a thickened ligamentum flavum, arachnoiditis, subarachnoid hemorrhage following trauma, and rarely diabetic neuritis, syringomyelia and multiple sclerosis. It is not within the scope of this paper to discuss in detail the diagnosis of each of these conditions.

The presence of a ruptured intervertebral disk has been suspected in a number of the spondylitic patients in this series. Two of them (Q M and W N B) had negative lipiodol reactions, and in 1 (Q M) a negative exploration of the spinal canal was carried out at another hospital because of a suspected ruptured intervertebral disk. The clinical differentiation should as a rule be relatively easy. In the case of a ruptured intervertebral disk, the onset is usually acute, and a history of injury is

present in about 80 per cent of cases,^{15, 16} absent or diminished ankle jerks in 50 to 70 per cent,^{15, 16} anesthesia or hypoaesthesia of the leg or foot in 35 per cent^{15, 16} and a positive lipiodol reaction in over 90 per cent.^{15, 16} On the other hand, in patients with spondylitis the onset is insidious, a history of injury is infrequent, neurologic abnormalities are uncommon, and the lipiodol reaction is negative.

The diagnosis of rheumatoid arthritis of the spine is frequently missed because the examiner is not cognizant of its symptoms and signs. In fact, a careful history alone should often serve to differentiate rheumatoid spondylitis from a ruptured intervertebral disk. In addition to the symptomatology and signs of spondylitis previously mentioned, these patients frequently complain of pain in areas of the spine other than the lumbar and sacral regions. Their symptoms are always worse on awakening and associated with generalized stiffness. They rarely obtain relief on lying down. Most of them admit suffering from general malaise, easy fatigability, anorexia and weight loss, often preceding the onset of the articular symptoms. Finally, the characteristic roentgenographic changes in the sacroiliac joints (narrowing, irregularity, haziness, decalcification and increased bone formation, occurring alone or simultaneously and eventually leading to fusion) usually occur early in the disease. Occasionally, the history, physical findings, and cerebrospinal fluid and roentgenologic examinations are not sufficiently characteristic to allow one to make the diagnosis. In such cases only the passage of time will allow for progression of the disease and the establishment of the correct diagnosis.

SUMMARY

The cerebrospinal fluids from 101 patients with rheumatoid arthritis, 42 having spondylitis with or without peripheral arthritis, and 59 having involvement of the peripheral joints alone, were examined.

The only significant abnormalities observed were increased protein contents, abnormal colloidal-gold curves or a combination of the two.

Nine, or 12 per cent, of the 59 patients with rheumatoid arthritis involving the peripheral joints alone and 16, or 38 per cent, of the 42 patients with spondylitis exhibited such abnormalities.

Fifteen of the 16 patients with increased cerebrospinal-fluid protein had either spondylitis or symptoms suggesting spinal involvement. This fact points strongly to a relation between an elevation of the spinal-fluid protein and the presence of rheumatoid arthritis in the spinal and sacroiliac articulations.

Cerebrospinal-fluid alterations occurred more frequently in the spondylitis patients with severe pain or sciatica or both and hence presumably with a higher degree of inflammatory activity.

Factors probably involved in the production of these abnormalities are alterations in the serum proteins and increased permeability of the meninges from their proximity to inflamed articular tissue.

Attention is called to the diagnostic difficulties presented by patients with rheumatoid spondylitis and increased cerebrospinal-fluid protein, with particular reference to their differentiation from cases with ruptured intervertebral disks.

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MEDICAL PROGRESS

THE MECHANISM OF HEART FAILURE AND RELATED STATES (concluded)*

LAURENCE B. ELLIS, M.D.†

BOSTON

Circulatory Changes Subsequent to Treatment

It has already been brought out that as a result of the treatment of congestive failure with digitalis and other measures, the cardiac output usually improves, although not to the level that existed prior to failure. Harrison,³⁵ however, has emphasized that this improvement in volume flow is not invariable nor does it bear any close relation to the change in clinical symptomatology; and Starr⁹ has published examples of improvement in heart failure accompanied by a decrease in output. Starr has also presented data obtained with the ballistocardiogram indicating that the initial dose of digitalis may produce a temporary increase in cardiac output greater than that which persists when the full digitalizing effect is obtained.

The well-known value of the application of multiple tourniquets in the treatment of acute pulmonary edema is given objective experimental confirmation in the studies of Ebert and Stead,³⁶ who show that the application of such tourniquets can result in a temporary diminution in the circulating blood volume averaging 720 cc., and that this measure is thus temporarily the equivalent of a good-sized venesection.

Certain changes observed with the onset of diuresis have been discussed in the previous section. Proger, Ginsburg and Magendantz,³⁷ Schroeder,³⁸ Schemm³⁹ and Ellis⁴⁰ have shown the value of restriction of sodium in the diet in controlling cardiac edema.

The rationale for weight reduction in heart disease receives confirmation in the work of Master et al.,⁴¹ who have demonstrated that the oxygen consumption, cardiac output and cardiac work are diminished when overweight subjects undergo weight reduction. Proger and Magendantz⁴² had previously shown a reduction in cardiac output and cardiac work of patients with congestive heart failure subjected to prolonged dietary restriction.

Subnormal Circulation and Neurocirculatory Asthenia

A clinical picture that has posed a problem to physicians is that of patients who complain of weakness, giddiness when upright, fainting and a host of related symptoms. Some such patients are chronically troubled by these complaints and are usually labeled as having neurocirculatory asthenia; in others the symptoms develop only during or after an acute infection or some other debilitating disease. It has long been recognized that in such patients the circulation is inadequate. Starr and Jonas⁴³ have recently shown by ballistocardiographic studies that many of these patients, together with many elderly people with arteriosclerosis, and patients with coronary disease and with heart block, have inadequate cardiac outputs. The diminution of cardiac output in many of these patients, especially those with neurocirculatory asthenia and the postinfectious group, is not necessarily on a cardiac basis, but may well be due to inadequate peripheral compensation and poor return of blood to the heart. Starr has, however, also demonstrated that some patients, likewise diagnosed as having neurocirculatory asthenia, whose symptoms are somewhat similar have normal or increased cardiac outputs, and he suggested a separation of the two types. The symptoms of the latter group in many ways resemble Graves's disease. They complain of nervousness, tachycardia, palpitation, dizziness and dyspnea on exertion. The underlying etiology of the disturbed circulation in patients with neurocirculatory asthenia is of course not clarified by these investigations. The disturbance is probably due to central autonomic nervous stimuli arising in patients who are constitutionally predisposed to react in this fashion when under strain.

Shock and Cardiac Failure

What in many ways is an extreme and acute aggravation of the type of symptoms previously described as exhibited by patients with a subnormal circulation is the clinical picture usually called shock or peripheral circulatory collapse—extreme weakness, stupor, sweating, cyanosis, cold extremities, drop in blood pressure and so forth. It is

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generally believed that this is essentially a phenomenon of disturbance of the peripheral circulation, with a disproportion between the capacity of the peripheral vascular bed and the circulating blood volume. Some recent work has indicated that in certain circumstances an element of heart failure may be involved. Ebert and Stead⁴⁴ have presented evidence that in the shock picture occurring terminally in overwhelming infections there is little or no diminution in plasma volume and the venous pressure is relatively well maintained, and they believe that injury of both the heart and the peripheral circulation is involved. The same authors⁴⁵ have also carried out studies suggesting that a similar shock syndrome occurring in patients with acute myocardial infarction or chronic congestive failure may be due to cardiac failure alone.

Wiggers and Werle⁴⁶ found that the heart as well as the peripheral circulation may be involved in experimental shock. They state:

The capacity of the ventricles to respond to a given venous pressure is reduced, perhaps due to a prolonged reduction in coronary blood flow. The results strongly suggest that this is one of the factors which precipitate an irreversible circulatory state. Although the observations are limited to shock from a prolonged period of posthemorrhagic hypotension with reinfusion of blood, they nevertheless suggest that we may have accepted too hastily the theory that the myocardium is unimpaired in shock and that the course of circulatory failure cannot be benefited by the use of cardiac stimulants.

Circulatory Dynamics in Specific Types of Cardiovascular Disease

Fast and slow ventricular rates. Stewart and his co-workers⁴⁷ have shown that abnormal cardiac rhythms associated with fast ventricular rates, such as auricular fibrillation or flutter and supraventricular or ventricular tachycardia, are inefficient, leading to a decreased cardiac output per minute and per beat, dilatation of the heart and decrease in the amount of work done by it. On the other hand, slow ventricular rhythms, such as those that occur in high-grade heart block, are relatively efficient. Although the cardiac output per minute is somewhat reduced, the output per beat is greatly increased, the heart does not dilate, and the work accomplished is commensurate with the size of the heart.

Valvular heart disease. Stewart et al.⁴⁸ have made cardiodynamic studies that bear out the clinical impression long held regarding the degree of strain imposed on the heart by valvular lesions. Single lesions are not incompatible with normal function of the heart, but a combination of defects, such as mitral stenosis and insufficiency, is always,

according to their observations, accompanied by reduction in function. Patients with mitral disease and aortic regurgitation show less functional impairment than do those with mitral involvement alone; in other words, aortic regurgitation is of functional benefit. Aortic stenosis in combination with other lesions always results in marked decrease in function.

Bazett, LaPlace and Scott⁴⁹ presented observations on 2 subjects with free aortic regurgitation in whom the amount of blood regurgitated was 16.6 and 31 per cent, respectively, of the total ejected by the left ventricle. The total output of the left ventricle in this condition is thus greatly elevated and its work may be increased by 50 per cent or more.

Adhesive pericarditis and pericardial effusion. Stewart et al.⁵⁰ found that constrictive pericarditis results in a decrease in cardiac output and an elevation of venous pressure owing to interference with the inflow of blood to the right side of the heart and possible impairment of contraction. In another paper⁵¹ they reported essentially similar results in pericardial effusions. In both conditions with removal of the tamponade the cardiodynamics returned to normal.

Congenital cardiovascular defects. An important study by Eppinger, Burwell and Gross⁵² on 6 patients with uncomplicated patent ductus arteriosus brings out the astonishing fact that the amount of blood flowing through the patent ductus may be from 4 to 19 liters per minute, representing from 45 to 75 per cent of all the blood pumped by the left ventricle. The increased work load on the heart and especially on the left ventricle is obvious.

Stewart and Bailey⁵³ carried out measurements in 14 cases of coarctation of the aorta and found that the output of the heart was normal or even increased before the onset of failure. Because of the elevation of blood pressure in the aorta, the work of the left ventricle in these patients was increased. Nevertheless only 5 of the patients showed cardiac enlargement, and when this occurred the prognosis was poor. The nature of the hypertension in this condition has long been the subject of study and speculation. It has been held that it is neurogenic in nature,⁵⁴ but this has been denied (Pickering⁵⁵). Recently, as the result of Goldblatt's demonstration that chronic hypertension may be produced experimentally by reduction in renal blood flow, the thesis has been advanced that coarctation of the aorta is in essence a "Goldblatt clamp" that reduces renal blood flow, and that this in turn releases a hormonal vasoconstrictor mechanism. Evidence in favor of this belief is contributed by Friedman et al.,⁵⁶ who have

found a substantial reduction in renal blood flow in 6 patients with coarctation and by the experimental work of Ryland,⁵⁷ who obtained essentially similar results. If the hypertension of coarctation is similar to Goldblatt's experimental hypertension, one would expect a generalized vasoconstriction with increase in peripheral resistance, and not one limited to regions proximal to the aortic constriction. That this is indeed the case is suggested by the work of Steele,⁵⁸ who by direct measurements of intra-arterial pressure found that in the femoral arteries of such patients the diastolic pressures were elevated to an extent comparable to that in the arms, although the pulse pressures were unusually low.

Pulmonocardiac Failure

Although much attention has been paid in the Continental literature to "kyphoscoliotic heart disease," there has been comparatively little in English and American publications on this subject. Chapman, Dill and Graybiel,⁵⁹ however, have recently reported in detail the clinical and physiological features of this condition. Dyspnea, palpitation and fainting in patients with marked chest deformities are warning signs—signs unfortunately often mistakenly attributed to a neurosis. Although these patients may develop congestive failure of the usual type, this is unusual; sudden profound circulatory or respiratory collapse, frequently unresponsive to treatment, is common. The clinical state is different from that of the usual chronic cor pulmonale, or right-sided heart failure occurring in patients with chronic pulmonary disease such as emphysema, pulmonary fibrosis and so forth. The disturbed circulatory function in pulmonocardiac failure is dependent chiefly on interference with pulmonary dynamics—reduction in vital capacity, increase in residual air and inefficient pulmonary exchange of gases, with deficient arterial oxygenation, together with the great mechanical difficulty in respiratory movements.

Kerwin⁶⁰ reported 5 patients with pulmonocardiac failure in whom dyspnea and cyanosis were the most prominent clinical features. He pointed out what had been previously observed by Chapman, Dill and Graybiel and others, that hypertrophy and dilatation of the right side of the heart regularly occur, suggesting that chronic pulmonary hypertension had existed during life.

SUMMARY

Recent investigations concerning alterations in circulatory physiology that occur in various types

of heart disease and in heart failure are discussed especially as they bear on the explanation of clinical signs and symptoms. The numerous and complex factors concerned with the production and maintenance of clinical manifestations such as dyspnea or edema are brought out.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29101

PRESENTATION OF CASE

A fifty-two-year-old man entered the hospital because of abdominal pain.

Approximately four years prior to admission the patient first suffered from attacks of crampy abdominal pain that were relieved by belching and cleared spontaneously after several weeks. He remained quite well until one year before entry, when he noted mild exertional dyspnea, which became worse six months later and was associated with easy fatigability. At that time he "strained his back" and was confined to bed for one month, when the back discomfort completely cleared. Six weeks before admission he began to suffer from attacks of lower abdominal crampy pain that extended across the abdomen, but apparently had no further radiation. Occasionally, the pain made the patient double up. The attacks usually lasted five to fifteen minutes and occurred irregularly during the day. There was no relation to meals but at times the pain occurred after fatty meals. There was no associated nausea, jaundice, fever or chills. Soda occasionally provided some relief and at times the pain was relieved by voiding. The bowels moved regularly, but the patient had taken a cathartic every day during the three weeks prior to admission. The stools were never bloody, tarry or acholic but at times were rather loose. Three weeks before entry his abdomen began to swell and he had some distress in the right upper quadrant, which had no apparent relation to the lower abdominal pain. This continued to the time of admission. Two weeks prior to admission, orthopnea developed and the patient required three pillows for rest in bed. No leg edema had been noticed. He then developed a cough that was productive of small amounts of yellowish sputum; there was no chest pain, but he did complain of a sense of fullness and aching at the costal margins. During the illness he had lost approximately 20 pounds. During the five years prior to admission, the patient's diet was irregular and of poor quantity and quality. He often missed two meals during a single day. He denied any more than "one drink a week."

The patient's mother died at seventy-four of "cancer," and his father died at seventy-six of "stoppage of the bowel." The past history was noncontributory.

Physical examination revealed a well-built man who had lost a great deal of weight. He belched frequently but appeared to be comfortable. The heart and lungs were normal. The abdomen was distended and tympanitic. No masses were felt, and no tenderness was elicited. A fluid wave was demonstrable. The inguinal lymph nodes on both sides were enlarged, firm, discrete, nontender and freely movable.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 98.8°F., the pulse 90, and the respirations 20.

Examination of the blood revealed a hemoglobin of 13.2 gm. per 100 cc. and a white-cell count of 12,100. The urine was normal. The blood Hinton test was negative. The nonprotein nitrogen was 22 mg. per 100 cc., the chloride 97.7 milliequiv. per liter, and the protein 4.7 gm. per 100 cc. A flat plate of the abdomen demonstrated considerable air in a dilated stomach, but there was no evidence of dilated small or large bowel. There were numerous fine flecks of calcification that had the appearance of gall stones. The density of the abdomen was suggestive of fluid, but this may have been due in part to the patient's size. No air was seen within the biliary tree. A Graham test showed no filling of the gall bladder. There was dye in the stomach. A barium enema passed to the midsigmoid, where it met a complete obstruction. Insufficient barium passed the point of obstruction to demonstrate the type of lesion. There was considerable gas in slightly dilated loops of small bowel and in the descending colon.

An operation was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD L. YOUNG: The exertional dyspnea and easy fatigability could indicate an old man getting older, or they could suggest the beginning of cardiac failure.

"There was no relation to meals but at times the pain occurred after fatty meals." This is a suggestion of gall-bladder trouble, as are the pains spoken of earlier that were relieved by belching. Gaseous distention of the stomach may cause pressure on a damaged gall bladder, and hence pain, which may be relieved by belching.

Although not at all diagnostic, the fact that soda relieved the pain is again of interest. If you ask a patient how and he says, "It makes me belch gas," that also makes you think of gall bladder. The

relief of ulcer pain by soda is a chemical rather than a mechanical relief.

In spite of the fact that we are taught in school to consider one diagnosis for the cause of symptoms, one has only to look at the diagnoses going out from this department to realize that all the patients we are dealing with have more than one anatomic lesion. This patient may have had gall stones and some other condition more recently.

The commonest cause of weight loss is cancer. The patient also had a suggestive family history.

On physical examination the patient belched frequently. Ninety-nine out of a 100 patients who sit down before you and belch will prove, if you watch them carefully, to be cribbers.

"The abdomen was distended and tympanitic." The one who reported that ought to have been more explicit. If it was tympanitic everywhere there was no fluid wave. Of course if he had said there was tympany in the midline, dullness in the flanks, and a fluid wave we might believe it; but the man was of good size, with a big belly, and had lost weight, and I defy anyone to be sure of a fluid wave under such conditions.

The enlarged lymph nodes are possibly important, probably not. The protein was below the so-called "edema level."

"No air was seen within the biliary tree." That is an interesting observation. It makes one think that the examiner was wondering about gallstone ileus. The only way I know of explaining air in the biliary tree is by a direct opening from the gall bladder into the intestine, which is also the only way a large gallstone gets into the intestine. Under these conditions we do occasionally see air in the biliary tree. Would you say that was so, Dr. Holmes?

DR. GEORGE W. HOLMES: Yes.

DR. YOUNG: We are not told about occult blood in the stool. Is that important? We are entitled to ask if there was enough coming from the bowel to test for occult blood. Of course we are given the strong suggestion that this man had gallstones. I am going to ask Dr. Holmes if he would be willing to be more explicit.

I do not believe we have any right to consider gallstone ileus on the basis of this story because the obstruction was in the midsigmoid. I have never known a gallstone to make trouble at that point. A gallstone can make trouble at various places in the small bowel, where it acts as an obturator. It often goes to the ileocecal valve and there makes trouble. Although the patient may have had gallstones, I do not believe they are the cause of his trouble.

In a man of this age coming in with a story of crampy pains and this appearance in the x-ray

films, one first has to settle whether there is an obstruction that requires operation. Let us immediately say, "Yes." Then Dr. Mallory will ask what it was due to. The patient was fifty-two years old and may well have had malignant disease. That is always the first thing to consider. Malignant disease can fit this picture throughout—the crampy pains going on for a brief period beforehand, the slight loss of blood and the anemia.

What other things should one think of? We have thrown out gallstone ileus. I shall be arbitrary and say that it is not that. Could it be tuberculosis? The patient had questionable fluid in the belly. That either came from metastatic malignancy of the peritoneum or from tuberculosis. I doubt if it was tuberculosis for such lesions are commoner on the right side, in the region of the ileocecal valve. They do occur with some frequency on the left side, often enough so that we ought to consider tuberculosis. Diverticulitis could account for these symptoms but not for fluid in the peritoneal cavity. It could account for the white-cell count, which is slightly elevated, and a localized diverticulitis may have been the cause of the trouble, even though no diverticula were seen in the x-ray films. I cannot throw out the diagnosis completely.

What else is there? Intussusception gives a characteristic rectal discharge of mucus and prune-juice material; I believe that its absence rules out the diagnosis. Then there is the question of a large polypoid leiomyosarcoma, which is rare.

In other words this comes down to a question of obstruction due to malignant disease, diverticulitis or a combination of the two. Please remember that they can occur together. The important thing is what to do. There is one other thing we see about once a year in the hospital, namely, old people with merely a fecal impaction. We do a cecostomy, and when the smoke has cleared away we have nothing else to account for the difficulty. The thing to do here is to relieve the obstruction. Going merely on the theory of chances, I shall say that the cause was carcinoma of the sigmoid, with diverticulitis the second choice. It will not hurt my feelings to have it prove to be the second, but it will hurt my feelings to have it prove to be anything but one of these two. I should like Dr. Holmes to add anything he can from the x-ray films.

DR. HOLMES: There is positive evidence of gallstones, but there is nothing to make me think of gallstone ileus. In the first films there is little evidence of gas in the abdomen, and the more or less ground-glass appearance of the abdomen suggests the presence of a considerable amount of fluid. At no time was there an excessive amount

of gas in the small bowel. At one time the stomach was considered dilated with gas and there was more or less gas in the large bowel.

One thing of interest is that at no time was there much gas in the rectum.

DR. YOUNG: Was there loss of mucosa in the obstructed area?

DR. HOLMES: I do not believe so. I agree with the record: all that one can say is that the patient had obstruction. That is surprising. In diverticulitis or carcinoma, one can usually guess what the cause of the trouble is. These films, however, give no evidence other than that of obstruction.

DR. YOUNG: I might mention hernia, volvulus and other things, but I do not believe they deserve serious consideration.

DR. FLETCHER H. COLBY: I should like to ask Dr. Young if diverticula are apt to cause complete obstruction.

DR. YOUNG: No; but neither does cancer. There is generally a trickle to give a clue.

DR. HOLMES: That is true.

DR. REGINALD H. SMITHWICK: What is the level of the obstruction?

DR. HOLMES: It is near the rectosigmoidal junction.

DR. SMITHWICK: Do you think it is beneath the peritoneal inflection?

DR. HOLMES: I cannot answer that.

CLINICAL DIAGNOSES

Carcinoma of sigmoid.
Carcinomatosis peritonei.

DR. YOUNG'S DIAGNOSES

Carcinoma of sigmoid.
Carcinomatosis.

ANATOMICAL DIAGNOSES

Carcinoma of gall bladder, with regional metastases and diffuse peritoneal implantation.
Obstruction of sigmoid by adhesions.
Ascites.
Pulmonary edema.
Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was explored, and a presumably primary tumor was found in the region of the sigmoid. It was apparently thought that the degree of obstruction was not severe enough to necessitate a colostomy; so a specimen was taken and the surgeon backed out without doing anything more. The patient gradually accu-

mulated more and more ascitic fluid, slowly failed and died.

Autopsy showed that the gallstones were directly connected with the intestinal obstruction but not in the form of gallstone ileus. The gall bladder contained many small stones, as Dr. Holmes pointed out, and one of the dangers of symptomless stones in the gall bladder is that they may induce carcinoma. There was a primary cancer of the gall bladder, a characteristic polypoid growth within the lumen of the organ. It had invaded the liver extensively and had metastasized to the lymph nodes around the head of the pancreas; at first there seemed to be cancer of the pancreas, but on dissection it became clear that the pancreas was surrounded by tumor but uninvolved. There were generalized peritoneal implantations, and these were most marked in the dependent portions of the abdomen. In the pelvis the cancer had grown in a diffuse sheet over the serosa of the sigmoid, anchoring it in the shape of a sharp S. The obstruction was due to the kinking rather than to anything else. The mucosa was uninvolved and it was quite possible to follow around the curves one at a time with an instrument, but functionally it was, as has been said, a fairly complete obstruction.

DR. YOUNG: How much fluid was in the belly?

DR. MALLORY: There were many encapsulated pockets of fluid, each quite separate from the other.

DR. YOUNG: Was this a separate tumor in the sigmoid or was it a metastatic tumor from the gall bladder?

DR. MALLORY: It was a peritoneal metastasis from the tumor in the gall bladder.

A PHYSICIAN: How about the lungs?

DR. MALLORY: They showed massive pulmonary edema, which was, I am sure, a terminal complication. The heart was normal.

DR. HOLMES: Was this man peritoneoscoped?

DR. MALLORY: No.

CASE 29102

PRESENTATION OF CASE

A forty-six-year-old Greek machinist entered the hospital because of swelling of the abdomen.

Six months prior to admission the patient noticed the onset of ankle edema. This became progressively worse, and three weeks before entry his abdomen began to swell. At that time he lost his appetite, felt nauseated and frequently vomited everything that he ate. His family noticed that he had lost his ruddy color and seemed yellow. This color deepened during the second week of his

illness but during the week prior to admission it began to fade. During the three weeks before entry he had had diarrhea four or five times a day, usually after eating, and his stools were described as yellowish but never clay colored. His diet was limited to milk and soups during this period. He developed an irritating nonproductive cough, and dyspnea requiring two pillows at night. The urine became dark, but this was unassociated with urinary symptoms other than nocturia (four or five times), which he had had for a year. Pain was not a prominent feature of the illness, but three weeks before entry he experienced a vague discomfort in the right back. During the next week he had occasional attacks of knifelike pain radiating from both flanks to the umbilicus, and later he had upper abdominal pain that radiated around to the back on both sides. The longest attack lasted two hours.

The patient consumed only a "moderate" amount of alcohol, and more than a jigger or two daily. There was no history of exposure to industrial solvents.

The family and past histories were noncontributory.

Physical examination disclosed a thin man who was not in obvious distress despite a markedly distended abdomen. The skin was dark and sallow. The scleras were yellow tinged. The diaphragm was high, particularly on the right. There were scattered crackling inspiratory rales at both bases of the lungs. Examination of the heart was negative. The abdomen was markedly distended and tense. A fluid wave was easily demonstrated and there was shifting dullness in both flanks. The liver edge was palpable 7 cm. below the costal border, and the edge was smooth. There was pitting edema of both lower extremities to the knees.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 99°F., the pulse 100, and the respirations 22.

Examination of the blood revealed a red-cell count of 6,400,000 with a hemoglobin of 90 per cent, and a white-cell count of 6000, with 81 per cent polymorphonuclear leukocytes. The urine was acid in reaction, had a specific gravity of 1.024 and showed a +++ test for bile; the sediment contained 8 to 10 white cells per high-power field. The blood Hinton test was negative. One stool gave a +++ guaiac test, but two later examinations were negative. The van den Bergh was 3.8 mg. per 100 cc., direct, and 6.2 mg., indirect. The serum nonprotein nitrogen was 22 mg. per 100 cc., the chloride 97.7 milliequiv. per liter, and the protein 8.1 gm., the albumin 2.3 gm. and the globulin 5.8 gm. per 100 cc., making an albumin-globulin ratio of 0.4. The prothrombin time was 32 seconds (nor-

mal, 20 seconds). The cephalin flocculation test was ++ at 24°C. and ++++ at 40°C. A barium meal of the upper gastrointestinal tract showed marked curling of the lower esophagus; this area was slightly irritable and regurgitation occurred. A hiatus hernia measuring 2 by 2 cm. in diameter was seen, but there was no evidence of varices. The stomach was not remarkable. The duodenum and small intestines appeared normal so far as seen; however, examination was handicapped by the large amount of ascites. A barium enema passed from the rectum to the cecum without delay. There was no evidence of intrinsic disease in the rectum and colon. There appeared to be some depression or displacement of the sigmoid inferiorly, and the ascending and descending colon lay well laterally. No soft-tissue mass was demonstrated.

In spite of supportive treatment and paracentesis the patient failed rapidly. He became unable to retain any food or fluids. A flat plate of the abdomen after paracentesis demonstrated a markedly enlarged spleen. The lower aspect was not visible because of overlying intestinal gas. However, it reached almost to the level of the iliac bone. The shadow of the liver was apparently not enlarged. The patient died on the thirteenth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. REED HARWOOD: I am sorry there is no roentgenologist here. "Curling" of the esophagus is supposedly due to adhesions and is of no particular significance except that it may sometimes be confused with esophageal varices. Esophageal varices were not demonstrated in this case. I should like to ask if the spleen was palpated after paracentesis, and if it did reach down as far as the iliac bone. The record indicates that the spleen was enormous, yet I see the iliac crest here and what I take to be the lower border of the spleen lies considerably above it. Would you agree with me, Dr. Jones, that the spleen is large but not enormous?

DR. CHESTER JONES: The stomach shadow appears to be pushed over to the midline. It is hard to be sure, but I should agree that the shadow you indicate is probably spleen. There was so much fluid in the abdomen when that film was taken that many outlines are obscured.

DR. HARWOOD: Another question I should ask the roentgenologist is, Do you think the spleen has pushed the descending colon laterally?

DR. CHESTER JONES: It does not show it in this film.

DR. HARWOOD: I should like to know how the roentgenologist interprets a finding of that sort. It may be significant.

DR. JONES: The two flexures seem to be in about the same position.

DR. HARWOOD: With you as my roentgenologist, Dr. Jones, I am going to take the liberty of discounting the statement that the descending colon was pushed laterally.

In summary we have the case of a patient who had edema, ascites, marked splenomegaly, jaundice, an inverted albumin-globulin ratio and a positive flocculation test. All these point strongly to severe liver damage. My first thought on reading the case over was that the patient had cirrhosis with a rapid progression, perhaps a toxic hepatitis. There are several points that are not entirely consistent with this diagnosis and I shall discuss these at some length.

The spleen, at least according to the interpretation of the X-ray Department, was unusually large for a case of alcoholic cirrhosis. As I read the record, it reminded me of the type of spleen one gets in Banti's disease. However, Banti's disease is a chronic ailment associated with marked anemia, and usually appears in people considerably younger than this man. Then again the jaundice is rather too marked for the ordinary case of alcoholic cirrhosis. However, in a case that is progressing rapidly with marked liver damage, jaundice of this degree could be expected to appear. Then we find that there were no esophageal varices. In alcoholic cirrhosis with a severe degree of ascites and a large spleen one would expect also to find esophageal varices. In addition, the history does not give us the usual immoderate intake of alcohol. However, many cases of cirrhosis in which the alcoholic intake was slight have been presented in this room.

The high serum protein is disturbing. In cirrhosis and most liver diseases the serum protein tends to be low, both the albumin and globulin being diminished, but the albumin to a greater extent. We are taught to think at once of multiple myeloma when we see a high serum protein. Multiple myeloma occasionally involves the spleen. However, I do not know of any cases in which ascites and jaundice were also present, so I am inclined to say this patient did not have multiple myeloma.

I am told that in the early stages of cirrhosis of the liver the serum globulin can be high and that only in the later stages does it become lowered, so this finding may be confirmatory evidence of the diagnosis of cirrhosis. The interval between the onset of the ascites and death is rather short for the usual case of chronic alcoholic cirrhosis. However, cases can progress as rapidly as this. Finally there is a high red-cell count (6,400,000) and a hemoglobin of 90 per cent. These are dis-

tinctly unusual findings in cirrhosis of the liver, in which anemia is the rule. It may be the clue to the diagnosis. I should like to ask Dr. Mallory if that was repeated and still found to be high.

DR. TRACY B. MALLORY: It was done on only one occasion.

DR. HARWOOD: Perhaps I should not put too much emphasis on that point. It is possible that the patient was dehydrated and had a certain degree of hemoconcentration as a result of his inability to take fluid and as a result of his diarrhea.

The record states that the patient had a ruddy color. Ruddy color and a high red-cell count, with a spleen that seemed rather larger than one would ordinarily expect in cirrhosis, make one think seriously of the diagnosis of polycythemia vera. We know that, in polycythemia vera, thromboses in various vessels are of common occurrence, particularly in the mesenteric vessels. I have not actually heard of a case of portal thrombosis in polycythemia, but at least it is conceivable that this man had portal thrombosis of gradual onset and progression, resulting in ascites, liver damage and death. The main objection is that in portal thrombosis the signs of ascites are also accompanied by marked hematemesis and even more rapid progression than in this case. Another objection to the diagnosis of polycythemia is that the red count was not extremely high. I should feel that I was on surer ground if the red-cell count had been 8,000,000 or 9,000,000. Finally, the patient did not have any of the other signs of polycythemia, such as cyanosis, distended veins and so forth. In any event I think it is a possibility. Other conditions, such as lymphoma and carcinoma of the liver, I have also thought of and discarded, because most of the signs seem to point toward a toxic hepatitis, and I shall make that my final diagnosis and just raise the question of the possibility of polycythemia with thrombosis of the portal vein.

DR. WILLIAM B. BREED: The absence of a roentgenologist gives us a golden opportunity to talk freely about these x-ray plates. I am not convinced that these pictures show merely "curling" of the lower end of the esophagus, and I should like to have someone convince me that this does not represent varices of the lower part of the esophagus. I have had occasion to review similar pictures with the roentgenologist and from time to time have persuaded him to reverse the decision. Can anyone discuss this a little more intelligently than I can? Dr. Jones, what do you think about it? How often do you see "curling" of the lower end of the esophagus? It seems an inadequate term and it does not look like curling to me. Would you say definitely that there were no varices?

DR JONES In the left hand film there is 'curling' and no suggestion of varices. In the third film to the right there is a slight suggestion of varices. It is sometimes possible by turning the patient to bring out a change in the esophageal contour. We find varices in about 40 to 50 per cent of our cases of cirrhosis. I am sure that the absence of demonstrable varices does not rule out cirrhosis of the liver. I think at times it is important diagnostically for a roentgenologist to say there are or are not varices. The right hand film certainly shows something suggestive of varices.

DR EDWARD B. BENEDICT Extensive varices give filling defects.

DR BREED I acknowledge that they are not extensive, but I should like to give Dr Harwood support.

DR JONES He certainly has enough evidence of intrahepatic involvement from the laboratory point of view. Whether that is the whole picture, I do not know.

DR JOSEPH AUB I am beguiled by the high globulin. It is a rare finding and I wonder if sarcoid should be considered.

DR JONES I should say that hyperglobulinemia is rather the rule in liver disease, and that low serum protein is not necessarily the rule. I have recently looked up 50 cases of cirrhosis, most of the patients showed a normal total protein, and the normal figure was usually due to a high globulin. Therefore the serum protein figure by itself is not too significant. It is the albumin globulin ratio that is important. Certainly, in the vast majority of patients with cirrhosis of the liver, if there is ascites or edema, there is an elevated globulin and an inverted ratio.

DR MALLORY A few months ago we had a meeting to discuss the possibility of eliminating unnecessary laboratory tests, and the question came up whether it was worth while to do albumin globulin ratios. Dr Butler was inclined to think they were rarely significant. Would you defend that statement, Dr Butler?

DR ALLAN M. BUTLER I can attempt to. But before defending it, I should like to ask one question. I notice that this patient was a Greek, and I remember Dr John Homans presenting a Greek patient, and saying that whenever you have such a patient remember he may have lived in Greece and may have come in contact with dogs and sheep. This fellow obviously had liver disease and a high globulin, and I wonder if he had lived in Greece and whether we should be thinking of echinococcal disease.

DR MALLORY He was born in Greece. There is no statement concerning how long he had been in this country.

DR BUTLER Now to defend the statement about determining albumin globulin ratios for the duration of the war.

The albumin globulin ratio is really only a qualitative analysis. Howe,* in 1921, said that 22 per cent of sodium sulfate precipitates the globulin and leaves the albumin in solution. Actually, when you precipitate any protein by increasing the salt concentration you get a logarithmic curve. If you take serum globulin and run a precipitation curve with increasing concentrations of sodium sulfate you find that with a concentration of 22 per cent all the globulin has not been precipitated. So at that particular sulfate concentration you have only a qualitative separation of albumin and globulin as some globulin remains in solution with the albumin. The next thing that makes it qualitative is that the sodium sulfate is supersaturated at room temperature. You have to keep the reagent in an incubator at 37°C to keep the salt in solution. When the technician pipettes the sulfate solution at room temperature, sodium sulfate in varying amount crystallizes out on the pipette. The amount varies a great deal with the care of the particular technician. Thus unless analyses are done carefully there is a technical error as well as a theoretical error. These factors limit the value of the routine determination of albumin globulin ratios.

Concerning the diagnosis, I think we all know that this patient had liver disease, even without the albumin globulin ratio. If any patient has liver disease and has edema too, we can guess that he has a low albumin and maybe has a low total serum protein. This latter can be determined accurately by one of several simple procedures. If the serum protein is high and edema is present, we know that the albumin is low. We do not need to do an albumin determination. Thus in such a case the albumin globulin ratio does not help a great deal. However, it may help in the rare case when one does not know whether the liver disease is serious. There was a girl presented at medical rounds six weeks ago who, from her story, might have had ordinary catarrhal jaundice. The albumin globulin ratio, however, was 0.2. That provided one of the pieces of evidence that led us to believe that the girl had something more serious than catarrhal jaundice. I do not know what happened. Do you, Dr Jones?

DR JONES She is still critically ill.

DR BUTLER In that case the albumin globulin ratio was an important factor in appreciating the seriousness of the illness. There are such rare cases in which the ratio is helpful. But to turn around and do a ratio on every patient who has

*Howe, P. E. Use of sodium sulfate as globulin precipitant in determination of proteins in blood. *J. Biol. Chem.* 49:93-107, 1921.

liver disease and ascites, or on every nephritic patient who has albumin in the urine, is not helpful enough to justify the analysis at a time like the present when we are trying to cut down laboratory work.

DR. JONES: I am in accord with Dr. Butler. In almost every case of liver disease the diagnosis is made first and the laboratory test subsequently. I think there is justification for doing this test for prognostic purposes.

CLINICAL DIAGNOSES

Toxic cirrhosis.

Hepatoma?

DR. HARWOOD'S DIAGNOSES

Alcoholic cirrhosis.

Toxic hepatitis.

Polycythemia and portal thrombosis?

ANATOMICAL DIAGNOSES

Cirrhosis of liver, type undetermined.

Hepatoma.

PATHOLOGICAL DISCUSSION

DR. MALLORY: There is a rare type of case in which one must decide whether ascites is due to

portal obstruction or to caval obstruction. In such cases the albumin-globulin ratio may be an important differential point.

This patient was peritoneoscoped by Dr. Benedict, who found a cirrhosis of unusual nodularity. Some of the nodules were a little peculiar in color and appearance so that Dr. Benedict suspected the possibility of tumor; however, he was unable to make a definite diagnosis. A biopsy of one of the nodules showed a hepatoma. Not long ago we had another case of hepatoma which had grown up the hepatic vein, as this tumor characteristically does, to form a tumor thrombus in the cava. In that man there was severe ascites in spite of a normal serum protein and a nearly normal albumin-globulin ratio. I thought the presence of a normal albumin-globulin ratio might have led one to suspect caval thrombosis by pointing toward a mechanical reason for the anasarca. In this case we have no evidence whether or not the cava was obstructed.

DR. HARWOOD: Were there any esophageal varices?

DR. MALLORY: We do not know; permission for an autopsy was not obtained.

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MENINGOCOCCAL INFECTIONS

SINCE cerebrospinal fever was first recognized in 1805 this disease has been known to occur almost constantly in a sporadic form and has assumed epidemic proportions at irregular intervals. It has flourished particularly during wartime both in the military and in the civilian population. Unlike such diseases as influenza, the outbreaks of meningitis are not explosive in their appearance and do not affect a large number of people. Rather, they begin insidiously, usually increase gradually and persist for several months and often for years, but never have a high attack rate. In England during World War I there were 300 cases in 1914, 2343 cases in 1915, 1278 cases in 1916 and 1395 cases

in 1917. The case fatality rate during these years averaged about 65 per cent. In the United States Army during these years there were 5939 cases, with a mortality of about 40 per cent.

The present war has seen an even greater increase in the number of cases of this disease in Britain, where a total of 12,500 cases occurred during 1940. There has also been a marked increase in the occurrence of this disease in Canada, particularly in Nova Scotia, and, more recently, many cases have been reported in this country, particularly in New England and in neighboring states. Even greater numbers of cases are to be expected in the near future.

Compared with previous outbreaks, the present one shows several striking differences, which should be borne in mind in view of the serious attitude that health officers and the general population assume toward this disease. In addition to the low incidence of meningococcal meningitis both in the general population and among the military personnel, the case fatality rate is now surprisingly low. In Britain less than 10 per cent of all the cases occurring in the general population end fatally. In most large series of cases that have been reported, particularly those derived mainly from military sources, the mortality is more nearly 5 per cent. Young infants and aged persons still account for the greatest number of the deaths among civilians. In this country it is to be expected that less than 3 per cent of the cases occurring in army camps and less than 10 per cent of those occurring among the civil population will end fatally.

The great difference in mortality is, of course, due to the marked effectiveness of the sulfonamide drugs. Sulfadiazine is now usually recommended as the drug of choice but any of the other widely accepted sulfonamides, namely, sulfanilamide, sulfapyridine and sulfathiazole, are also effective. For the most favorable results these drugs must be given as early as possible in the course of the infection. In severe cases, particularly those in which the patient is already stuporous or unconscious, the first doses of drug should be given

parenterally. It may not be amiss, also, to emphasize the importance of the administration of fluids early in such cases since the dehydration resulting from lack of fluid intake and from vomiting may predispose to renal complications if the sulfonamide derivatives are given intravenously. Early diagnosis and early and intensive treatment are therefore highly important.

Another encouraging feature of the cases that have occurred recently is the almost complete absence of serious crippling complications in patients who are properly treated. This is in striking contrast to the high incidence of total deafness and blindness among those who survived attacks of cerebrospinal fever in previous outbreaks.

Finally, the present-day treatment is much simpler than before.* Lumbar puncture is now performed only for diagnosis or for the evaluation of the progress of therapy. Intraspinal injections of serum, with the severe complications resulting from their use, have now been completely and, it is hoped, permanently abandoned. Antimeningococcus serums, if given at all, are used only intravenously or intramuscularly in severe cases or when the disease fails to respond to chemotherapy alone. Most British physicians have completely abandoned the use of serums, but this may be due, in large measure, to expediency as well as to the excellent results obtained without them.

Several epidemiologic features are worth stressing. During periods when cases of meningococcal meningitis are prevalent there are numerous carriers of epidemic strains, particularly among the exposed population. In closed units, as in military barracks or even larger outfits, as many as 50 or even 75 per cent of persons may harbor meningococci in the nasopharynx without apparent infection. The factors underlying susceptibility to infection are not known.

There are, however, cases of meningococcemia without meningitis, which should be recognized and treated early since, if they remain untreated, the patients may develop meningitis. Such cases

are, of course, most prevalent in epidemic periods. All persons having unexplained chills, petechial or purpuric rashes and joint pains or swellings accompanied by intermittent fever and headache should be suspected of having meningococcal infections. In some cases the symptoms are entirely respiratory and nowadays are likely to be attributed to atypical or virus pneumonia. Whenever possible, blood cultures should be made during the febrile phase and sulfonamide therapy should be given early.

During every epidemic there are a small percentage of severe and fulminating cases, usually with extensive purpuric eruptions. Some of these patients, today, fail to respond to intensive therapy. Such cases will probably comprise most of the deaths unless new methods are discovered for treating these patients more effectively.

With regard to prophylaxis, there seems little reason to advocate any large-scale adventures in this field. In small, compact and self-contained military units where action is anticipated soon after a case appears or after a large number of carriers are discovered it may be possible to eliminate the carrier state by a short course of sulfonamide therapy. Such a procedure at present is neither warranted nor feasible for large units of the population.

It is most important to emphasize the early recognition of cases of meningitis and of the various forms of meningococcal infection in the absence of meningitis and to treat such patients early.

FLORENCE CRITTENTON LEAGUE

THE Florence Crittenton Mission, a national organization, was established sixty years ago to provide medical care and helpful guidance to the illegitimately pregnant woman, in an effort to protect society and the individual from the spread of immorality and disease. In the ensuing years "homes" have been established in sixty American cities. The Florence Crittenton League, the local chapter and the only one in New England, was founded fifty years ago. It consists of twenty-three

*Dingle, J. H., and Finland, M. Diagnosis, treatment and prevention of meningococcal meningitis: with a résumé of practical aspects of treatment of other acute bacterial meningitides. *War Med.* 2:1-58, 1942.

"circles" in and about Boston, whose members not only raise funds for the work of the League but also take an active interest in helping the girls and young women who come under its care.

The League maintains a home and hospital in Brighton, which is described in more detail elsewhere in this issue of the *Journal*, as well as the Welcome House, a protective home for girls from fourteen to sixteen years of age who have been exposed to unwholesome environments.

The phenomenon of illegitimacy is not new, nor is it confined to any race or clime. It has been recognized as both a medical and a social problem for innumerable years and has been studied from all angles by experts in many fields, but no complete solution has yet been found. Although war, curiously, has not increased the burden of the Florence Crittenton homes, proper care of the girl who must bear the burden of illegitimate motherhood still remains a problem, and all physicians should be aware of the fact that this type of assistance can be obtained in Boston and many other parts of the country.

MEDICAL EPONYM

SWIFT-ELLIS TREATMENT

This was described by Homer W. Swift (b. 1881) and Arthur W. M. Ellis (b. 1883) of the Rockefeller Institute for Medical Research, in the *New York Medical Journal* 96: 53-55, 1912

Our method is to withdraw blood after intravenous injections of salvarsan or neosalvarsan, separate the serum, and on the following day dilute it to 40 per cent with normal saline. It is then heated at 56°C for one half hour. By means of lumbar puncture, 15 cc of spinal fluid is withdrawn and then 30 cc of the diluted serum, warmed to body temperature, is slowly injected into the subarachnoid space. The foot of the bed is raised for about an hour after the treatment.

R. W. B.

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ELIOT HUBBARD, JR., M.D., *Treasurer Pro Tem.*

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BREECH DELIVERY: DEATH CAUSED BY TRANSECTION OF SPINAL CORD

Baby B was born to a twenty-nine-year-old primipara at full term. Labor lasted fifteen hours and terminated in a breech delivery; although details are not available, this was said to have been "easy and noninstrumental." The birth weight was 6 pounds, 2 ounces. No asphyxia or cyanosis was noted, but the infant did not move its legs and the arms were limp. The left arm regained some motion, the right remained completely flaccid. At four days there seemed to be some movement of the legs, which was thought to be voluntary. On the seventh day, a consultant noted tension of the fontanel and obtained bright blood by lumbar puncture. On the next day the child was transferred to another hospital.

On admission the infant had regained its birth weight, but was cold, apathetic and dribbling small amounts of urine and feces. The right arm was flaccid, and the left was held in partial flexion and internal rotation. The legs were slightly contracted at the knees without voluntary motion, but with automatic mass withdrawal on stimulus to the skin anywhere on their surface. Active knee jerks were obtained. No evidence of pain on pin-point stimulus was elicited anywhere below the neck, although usually such stimulus produced mass withdrawal of the legs. A slight facial asymmetry suggested paralysis on the right.

Two lumbar punctures during the week after admission produced grossly bloody fluid, which was thought to be due to trauma during the puncture. X-ray films of the spine showed no abnormality. It was thought that the infant had an injury to the spinal cord due to avulsion of the nerves of the right brachial plexus, with more or less complete transection of cord at the mid-cervical level. At first the child's temperature was distinctly subnormal; it then tended to rise and became irregular as aspiration of food and mucus, with resultant respiratory difficulty, increased. No changes occurred in the general neurologic picture, and the baby died eight weeks after birth, presumably because of aspiration pneumonia.

This cause of death was substantiated by autopsy, as was the neurologic lesion. There was avulsion of all the roots of the right brachial plexus,

with diffuse and practically complete transection of the spinal cord at the midcervical level. This injury was accompanied by a hemorrhagic infiltration of the distal portion of the cord, extravasated blood being found in decreasing amounts down to the level of the dorsal cord. No gross lesion of the brain or of its supporting structures or vascular supply was encountered.

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Middlesex University School of Medicine, 1933 Spon-
sor Edmund H Robbins, 334 Broadway, Somerville
- ZARELLA, ANTHONY G, 333 Main Street, Medford
Middlesex University School of Medicine, 1934 Spon-
sor Salvatore Scelso, 395 Commonwealth Avenue,
Boston

Alexander A Levi, *Secretary*
481 Beacon Street, Boston

NORFOLK DISTRICT

- ALLERS, OLGA E, 28 Wellesley Avenue, Wellesley
Woman's Medical College of Pennsylvania 1938
- AVERY, BENNETT F, 41 Allerton Street, Brookline
University of Michigan Medical School, 1926
- BURNS FRANCIS A, 84 Central Street, Foxboro
Middlesex University School of Medicine, 1934 Spon-
sor Thomas H O Toole, 11 Walpole Street, Norwood
- CURRIER, WILBER D, 17 Seaver Street, Brookline
University of Nebraska College of Medicine, 1938
- ELLIOT, HOWARD L, 14 Strathmore Road, Brookline
McGill University Faculty of Medicine, 1929
- EPSTEIN, IDA F, 275 Normandy Street, Roxbury
New York Medical College, 1937
- McKELL, DAVID M, JR., 94 Longwood Avenue, Brookline
Harvard Medical School, 1938
- SELIEMAN, ARNOLD M, 169 Rawson Road, Brookline
Harvard Medical School, 1939
- SHALETT, IRVING J, 1589 Beacon Street, Brookline
Middlesex University School of Medicine, 1928 Spon-
sor Louis F Curran, 409 Marlboro Street, Boston
- STOWELL, JOSEPH M, 10 Conant Road, Chestnut Hill
Tufts College Medical School, 1936
- TANSEY, JOSEPH L, 63 Orchard Hill Road, Jamaica Plain
Harvard Medical School, 1937
- VANDAM, LEROY D, 235 Park Drive, Boston
New York University College of Medicine, 1938

Timothy F P Lyons, *Secretary*
270 Commonwealth Avenue, Boston

NORFOLK SOUTH DISTRICT

- ANGELO, PETER J, 229 Washington Street, Quincy
Tufts College Medical School, 1941
- HOWLEY, EDWARD J, 39 Riley Avenue, East Weymouth
Tufts College Medical School, 1941
- RUBIN, FRANK F, 795 Southern Artery, Quincy
Middlesex University School of Medicine, 1936 Spon-
sor George D Dalton, 754 Hancock Street, Quincy

Robert L Cook, *Secretary*
38 Russell Park, Quincy

SUFFOLK DISTRICT

- ASSAD, FREDERIC C, 1 Bond Street, Boston
Middlesex University School of Medicine, 1934 Spon-
sor Christus A Pattajo, 10 Hollis Street, Boston

- BUTTS, VINCENT, 244 Meridian Street, East Boston
College of Physicians and Surgeons, Boston, 1929
Sponsor G Lynde Gately, 624 Bennington Street,
East Boston
- GIANTURCO, NICHOLAS D, 149 Hawthorne Street, Chelsea.
Middlesex University School of Medicine, 1934 Spon-
sor Lamar Soutter, 266 Beacon Street, Boston
- GILBERT, RAYMOND E, 850 St Marks Avenue, Brooklyn,
New York
Middlesex University School of Medicine, 1922. Spon-
sor Russell F Sheldon, 31 Pinckney Street, Boston.
- GORDON, ROBERT K, 44 Winthrop Street, Winthrop
Middlesex University School of Medicine, 1935 Spon-
sor Earle M Chapman, 266 Beacon Street, Boston
- HINDLE, WILLIAM V, 32 Queensberry Street, Boston
Harvard Medical School, 1937
- HITE JACOB W, 51 Park Drive, Boston
Middlesex University School of Medicine, 1930 Spon-
sor Louis E Wolfson, 113 Bay State Road, Boston
- INGERSOLL, FRANCIS M, 2 Poplar Place, Boston
Harvard Medical School, 1938
- KARP, ISADORE A, 153 Shurtleff Street, Chelsea
Middlesex University School of Medicine, 1936 Spon-
sor Frederick Ornsteen, 131 WASHINGTON Avenue,
Chelsea
- LIEBMAN, SUMNER D, 122 Riverway, Boston
Harvard Medical School, 1938
- RAMELKAAMP, CHARLES H, 66 East Newton Street, Boston
The School of Medicine of the Division of the Bio-
logical Sciences, University of Chicago, 1936
- ROIFF, HARRY S, 159 Shurtleff Street, Chelsea
St. Louis College of Physicians and Surgeons
Sponsor H Archer Berman, 475 Commercial
Avenue, Boston
- SAFFRAN, IRVING, Fort Lewis, Washington
Middlesex University School of Medicine, 1936 Spon-
sor David Fisher, 311 Commonwealth Street, Boston
- SILVEUS, ESTHER, 591 Beacon Street, Boston
University of Pittsburgh School of Medicine, 1937
- WALLACE, THOMAS E, 79 Payson Street, Boston
Middlesex University School of Medicine, 1936 Spon-
sor John T Williams, 429 Beacon Street, Boston
- YURKANIS, EDWARD F, 1654 Columbia Road, Boston
Middlesex University School of Medicine, 1936 Spon-
sor William R Morrison, 529 Commercial Street,
Boston

Holt's L. J. 1936, 1937, 1938
412 Beacon Street, Boston

WORCESTER DISTRICT

- BOYD, JAMES G, Box 289, Worcester
Boston University School of Medicine, 1936
- JOHNSON, WOLFRED, 140 Commercial Street, Worcester
Washington University School of Medicine, 1932
- NICHOLSKI, KASIMIR S, 15 North Main Street, Worcester
Middlesex University School of Medicine, 1936 Spon-
sor Benjamin F. 1936, 1937, 1938
Worcester
- MINSKY, JOSEPH W, 40 Commercial Street, West
Mid West Medical College, 1934 Spon-
sor 390 Main Street, Worcester

RICE, THEODORE A., 40 Whitman Road, Worcester.
Harvard Medical School, 1938.

Leslie P. Leland, *Secretary*
36 Pleasant Street, Worcester

WORCESTER NORTH DISTRICT

LAMB, MARSHALL A., 20 Walnut Street, Winchendon.
Tufts College Medical School, 1939.

SCHUCHTMAN, HAROLD I., 64 Milk Street, Fitchburg.
Middlesex University School of Medicine, 1934. Sponsor: Joseph D. Quinlan, 44 Prichard Street, Fitchburg.
Edward A. Adams, *Secretary*
44 Oliver Street, Fitchburg

DEATHS

BAILEY—WILLIAM T. BAILEY, M.D., of Boston, died January 16, in his seventy-fifth year.

Dr. Bailey received his degree from Harvard Medical School in 1900. He was a member of the Massachusetts Medical Society and the American Medical Association.

HARDING—EDWARD M. HARDING, M.D., of Newton, died December 19. He was in his ninety-first year.

Dr. Harding received his degree from the College of Physicians and Surgeons, New York, in 1874. At one time he served as second assistant physician at the Danvers State Hospital. He was a member of the Massachusetts Medical Society and the American Medical Association.

PHILBRICK—ROSCOE H. PHILBRICK, M.D., of New Orleans, Louisiana, died recently. He was in his sixty-third year.

Dr. Philbrick received his degree from Harvard Medical School in 1904. He was a member of the Massachusetts Medical Society and the American Medical Association.

TEMPLE—WILLIAM F. TEMPLE, M.D., of Boston, died December 25. He was in his fifty-sixth year.

Dr. Temple received his degree from the Harvard Medical School in 1911. He was past president of the Boston Society of Anesthetists. He served on the staff of the Massachusetts Women's Hospital. He was a member of the Massachusetts Medical Society and the American Medical Association.

MISCELLANY

NOTE

The commencement exercises of Middlesex University were held at New England Mutual Hall, Boston, on February 19. The degree of Doctor of Medicine was conferred on seventy-one successful candidates. Under the accelerated wartime program, instruction in the medical school will be resumed on March 17.

CORRESPONDENCE

FLORENCE CRITTENTON LEAGUE

To the Editor: May I call the attention of your readers to the facilities of our maternity home and hospital for the care of illegitimately pregnant girls and their babies.

The Florence Crittenton League maintains an ideal institution for the care of unmarried mothers—a unit home on the cottage plan with adequate hospital facilities surrounded with sufficient space for privacy to ourselves and to our neighbors. We also give expert care to girls who have the double misfortune of facing motherhood out of wedlock and of being afflicted with venereal disease. The physicians and social workers on the staff are experienced, and the Board of Directors is firmly convinced that the care rendered by the institution is unequaled. Hence, the Board is anxious to inform every community in New England, particularly in Massachusetts, that the maternity home and hospital exists and that we are prepared to help to the best of our ability the people of any community in matters connected with the problem of unmarried mothers.

The Florence Crittenton Home and Hospital, located at 10 Perthshire Road (Oak Square), Brighton, is the only institution of the Florence Crittenton Mission in New England. It offers prenatal, natal and postnatal care, and provides the following: cheery and comfortable rooms and dormitories for 23 expectant mothers; a hospital department including 21 beds with dental, operating-room and delivery-room suites; 33 cribs in sunny and well-ventilated nurseries and a completely equipped isolation unit consisting of 6 beds, a delivery room and a 6-crib nursery for the care of venereal-disease cases; expert medical, obstetric, pediatric and dental care in co-operation with the Boston Lying-in Hospital, Massachusetts General Hospital, Harvard Medical School and Forsyth Dental Infirmary; a large, sunny and airy 10-bed dormitory for convalescent mothers; a large, comfortably furnished living room for all classwork and recreation, with an adjacent well-equipped library; a fittingly furnished chancel adjoining the assembly room, which is opened for all devotional services; a social-service department with two trained workers, who help each girl and her family in making plans for her baby and her return to the community; and training under experienced workers in all household arts (cooking, nutrition, sewing and dressmaking), English, Red Cross home nursing, leather and metal tooling, and religious education. The charges are \$7 per week for board and \$30 for confinement, which are less than one third of the cost of the average case.

Applications should be made to the Superintendent, 10 Perthshire Road, Brighton, Massachusetts (STadium 7600). If a girl is refused admission, other sources of care are advised and she is followed by the case worker until plans are completed.

Our girls live with us for an average of five months. The mental, moral and physical care necessary for rehabilitation is obtained through a normal family life, which many of them have never known. Wholesome recreation is a vital part of our program, and includes dramatics, current events, reading and discussions, as well as special events for all holidays. Much follow-up work is done by the two case workers in helping the girls in their readjustments to the community and to the care of their babies. Such service is given to every girl as long as she needs help, and many of these friendly relations continue for indefinite periods.

CLARENCE R. PRESTON, *General Secretary*

88 Tremont Street
Boston

(Notices on page xi)

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TOXIC DUSTS, FUMES AND GASES IN INDUSTRY*

GEORGE E. MORRIS, M.D.†

BOSTON

DURING the year 1941, the Massachusetts Division of Occupational Hygiene was called on to furnish information concerning one hundred and twenty-four different industrial poisons,¹ receiving 1206 inquiries. Eighty per cent of these inquiries concerned the poisonous nature of the dusts, fumes and gases. Thus today my discussion concerns by far the greater part of the work done by this division.

Before taking up the industrial poisons in particular, it may be well briefly to discuss the avenues by which these substances get into the body. There are three main paths of entry, which in order of importance are the bronchopulmonary tree, the skin and the intestinal tract. It is to be emphasized that most industrial poisons enter the body through the lung fields in the form of vapors, gases or dust particles. Relatively few (mercury, nitroglycerin, nitrobenzene, tetraethyl lead, trinitrotoluene, the cyanides and possibly methyl alcohol) are absorbed by way of the skin, and fewer still by way of the gastrointestinal tract. Radium, manganese and cadmium are the chief ones admitted by the last method.

Not all people are equally susceptible to industrial poisons, for it is recognized that the young and the old are more prone to poisoning than are the middle-aged. Women are more susceptible than men, and pregnant women more than non-pregnant ones. People with heart disease usually react poorly to such agents as lead, nitrites, nitrates and the chlorinated hydrocarbons. Those with kidney disease are susceptible to poisoning by the heavy metals. Those with anemia do poorly when exposed to aromatic compounds. Alcohol addicts are in general poor risks.

So far as skin irritation is concerned, it can be said that colored skin is more resistant than white skin. Those with excessively oily skin often de-

velop dermatitis when exposed to cutting oils, waxes and substances soluble in fats, such as trinitrotoluene and tetryl. Those with dry skin are prone to develop dermatitis from solvents or powders.²

METALLIC DUSTS AND FUMES

Lead

The greatest amount of work done on any poison was carried out on lead. All physicians are acquainted with lead poisoning as it occurs in babies and in painters. However, from our records, lead poisoning is not considered in the differential diagnosis by physicians when they examine foundry workers, although such workers are almost invariably found to have abnormal amounts of lead in their urine. Lead is also a hazard in battery-room workers, junk-yard workers, those doing large amounts of lead burning or soldering and those engaged in salvage operations such as the cutting up of lead-painted steel structures.

Like most of the toxic substances that I shall discuss, lead is taken into the system mainly by inhalation. Only rarely is a case of poisoning by way of the gastrointestinal tract seen, and still less frequently does a case from skin absorption occur (tetraethyl lead is probably the only lead compound that is appreciably absorbed through the skin). Palsy, encephalopathy, arthralgia and colic³ are the four features that most textbooks require for a diagnosis of lead poisoning, but Kehoe⁴ found that in 30 patients with proved lead poisoning, only 1 had palsy and only 2 had encephalopathy. Twenty-one had arthralgia and 24 had colic. Thus palsy and encephalopathy can be dropped from discussion as diagnostic criteria. They are too infrequent to be of any value in diagnosis. Weakness, weight loss, constipation, abdominal pain, lead line and extensor weakness of the wrists are better criteria. Stippling of the red cells has not in my experience been found frequently enough to be of any value as a diagnostic aid.

*Read at the Postgraduate Institute, Massachusetts Medical Society, Boston, November 7, 1942.

†Physician, Division of Occupational Hygiene, Massachusetts Department of Labor and Industries; associate dermatologist, Boston City Hospital.

The Division of Occupational Hygiene has recently made 60 urinary lead determinations on girls engaged in manufacturing electrical products. These girls cut, grind and polish a plastic that contains an appreciable amount of lead. On casual inspection one would say that this process was not at all hazardous. Yet of the 60 urines analyzed, 35, or 58 per cent, showed abnormal amounts of lead. A complete study of these subjects is now being undertaken. It is not claimed that they have lead poisoning, but they are of interest because they are excreting and so must be absorbing abnormal amounts of lead. Since industrial medicine is primarily preventive medicine, the absorption and excretion of lead by workers before they show the signs and symptoms of disease are of great concern.

Recently I was called to a hospital outpatient department to see a man who complained of loss of appetite, abdominal pain, constipation and weakness of six years' duration. Gastrointestinal x-ray examination in 1936, 1939 and 1942 had shown duodenal spasm, but no ulcer. The patient proved to be a molder in a near-by foundry. In June, 1942, we had done air analyses at this foundry, and at that time the air contained lead far in excess of the maximum allowable concentration, which is 1.5 mg. per 10 cubic meters of air.⁵ A twenty-four-hour urine specimen of this foundry molder showed an excretion of 0.36 mg. of lead per liter. This is over four times the normal excretion (0.08 mg.). Here, then, was a man with a definite exposure, proved by analysis of the air which he breathed at work, symptoms referable to the gastrointestinal tract, x-ray findings of duodenal spasm and an abnormal excretion of urinary lead. It is not improbable that he had lead poisoning, and had had the same condition intermittently since 1936, though no such diagnosis appeared on his record.

A word should be said about the collection of urine in these workers. To do adequate lead determinations, a twenty-four-hour specimen is desirable, and one must be certain that the urine is collected in a container that has been washed with distilled, lead-free water. The patient must be instructed not to contaminate the urine with lead, for even small amounts introduced by accident will cause a wide error in the determination.

Antimony

The mention of lead automatically brings antimony to mind, for the two are extensively used in printers' type. Antimony is a metal that expands when it cools, and thus helps to maintain the size of the type. It is also employed in the

manufacture of storage-battery grids and of red-rubber compounds. Antimony salts have been used in the making of primer caps, and it is possible that they will be used again for this purpose. When antimony dust gets onto the skin it causes an eczematized dermatitis or a folliculitis. When inhaled or ingested it causes a metallic taste in the mouth, stomatitis, loss of appetite, nausea, vomiting, diarrhea, abdominal cramps and loosening of the teeth.⁶ These toxic symptoms are similar to those seen after the administration of tartar emetic or after the injection of antimony in the treatment of granuloma inguinale.

Antimony is often found mixed with arsenic, and in cases of poisoning it is difficult for the physician to decide which of these is the toxic agent. Arsenic poisoning need not be discussed here, since industrial poisoning from it differs very little from that occurring after the injection of antisyphilitic arsenicals.

Mercury

Mercury is used in the manufacture of explosives and of scientific apparatus. It is one of the few poisons that can be absorbed through the skin, as occurs in the mercury rubs given in the treatment of syphilis. Mercury is liquid at room temperature and volatilizes at 40°F. Thus fumes are found wherever the metal is left in open receptacles.

Symptoms of industrial mercury poisoning differ slightly from those seen when mercury is administered by injection or inunction. With the latter type of poisoning, there are a metallic taste in the mouth, stomatitis, a blue line along the gums, loss of appetite and diarrhea. In industrial poisoning, however, one also sees mental and neurologic manifestations such as timidity, discouragement, depression, insomnia, irritability and anxiety.⁷ Muscle tremors are frequent, at first fine but later becoming coarse. Normally no mercury is found in the urine, and over 0.25 mg. per liter is considered hazardous.⁸ Recently we made determinations on the urinary mercury content of 4 laboratory technicians who engaged in determining blood carbon dioxide and pH values. The mercury of the apparatus had been carelessly handled, and much of it had fallen onto the floor and into cracks in the tables and chairs. The workers were thus constantly inhaling mercury fumes emanating from the floor, chairs and tables. They were also absorbing mercury through the skin, for they were accustomed to play with the little mercury globules as they sat at the desks reading or writing reports. The respective urines of these girls showed 0.13, 0.19, 0.26 and 0.55 mg. of mer-

cury per liter. Thus it can be seen that even so small an amount as that spilled on the floor or on the tables in a technical laboratory can be hazardous. No symptoms of mercury poisoning had occurred in any of these subjects, but again the problem is to prevent such poisoning.

Manganese

Another metal of importance is manganese, which is used in alloys, dry batteries, silver solders and foundry work. It causes poisoning in a relatively short time, and cases have occurred after only three or four months of exposure. When any worker presents himself with a picture of multiple sclerosis, the diagnosis of manganese poisoning should be kept in mind, for the two diseases are clinically much alike. Such findings as languor, sleepiness, masklike facies, economical speech, cramps in the muscles of the legs, hyperreflexia, ankle and patellar clonus, retropulsion, propulsion and a slapping gait with a wide base are of common occurrence in both conditions. However, in manganese poisoning there are no eyeground changes, such as bitemporal pallor, and no spinal-fluid abnormalities. Poisoning is usually progressive and leads to disabling paralyses and permanent invalidism, but no shortening of life occurs.

Magnesium

This metal is used in foundry work, in aircraft manufacture and in the making of explosives. It is not a serious poison but causes a specific skin lesion, for when small particles penetrate the skin, a chemical reaction occurs and a specific type of foreign-body granuloma develops.⁹ Should much of the dust get into the mouth, it is probable that magnesium would act like other magnesium compounds, such as magnesium sulfate and magnesium hydroxide, causing purging and abdominal cramps.

Radium

Because of the sudden demand for radium-painted dials for airplanes, many workers are being exposed to the effects of radium. The dial-painters and the men who install the dials in instrument boards or work in the stock rooms where the dials are stored are equally exposed. An otherwise excellent book on industrial medicine³ casually dismisses radium poisoning by stating that its prevention has been shown to be a relatively simple matter, and refers the reader to a bulletin issued by the United States Bureau of Standards (Handbook H-27). On the contrary, it has recently been shown that, despite the finest ventilating equipment and the most meticulous workroom supervision, over a period of one year 3 of 100 girls working in a model radium dial-painting plant stored more

radium in their systems than is thought to be safe.^{10*} This safety value is probably in the vicinity of 0.1 microgm.¹¹ Radium poisoning was well known after World War I, when several radium dial-painters a few years after exposure developed osteitis, jaw necrosis, destruction of the bone marrow, anemia and sarcoma.¹²

Since the body cannot differentiate radium from calcium after absorption, much of the radium is excreted, but part of it is stored in the bones, where it bombards the marrow with alpha, beta and gamma particles. Such radiation at first stimulates the blood-forming tissues, but later fibrotic replacement occurs, and still later malignant neoplastic disease is prone to develop. It has been suggested that workers in this field be maintained on an adequate calcium, phosphorus and vitamin D diet for at least a month before going to work. In this way, much of the initial deposition of radium in the bones can be prevented.

It is to be remembered that radon differs from radium in that it is a gas and is taken in only by the bronchopulmonary tree. No absorption is thought to occur. Radon bombards the alveolar cells with radioactive emanations so that after many years, pulmonary carcinoma is apt to occur. The maximum permissible radon air concentration recommended in Massachusetts is 10^{-11} curies per liter.¹³

Fume Fever

Any of the heavy metals when in fume form can produce the syndrome known as metal-fume fever.¹⁴ Originally, it was believed that only zinc fumes caused this syndrome, but of late years it has become known that the fumes of lead, magnesium, and other heavy metals do so as well. The symptoms are thought to be due to the absorption of the foreign protein formed when the metal fumes come in contact with the alveolar cells and cause their necrosis. Some four to eight hours after exposure, the worker notices dryness in the throat, pains in the muscles and joints, weakness, chills and fever. The diagnosis of grippe or incipient pneumonia is often made on these workers. This syndrome is commoner in cold weather and on Mondays or after a day away from work or a vacation. The continued inhalation of the fumes seems to confer some immunity which is lost when the subject remains away from work for over thirty-six hours. No permanent disability has yet occurred from such inhalation, but it is to be remembered that if the fumes are from one of the poisonous metals, serious sequelae may result.

GASES AND VAPORS

By far the most important toxic gases and vapors are the volatile solvents, which now comprise

*This radium was subsequently eliminated by suitable treatment.

over three hundred and fifty different substances. The toxic gases and vapors are divided into asphyxiants, irritants and metabolic poisons, including the anesthetics and the volatile solvents.

Asphyxiants

The asphyxiants may be classified as physical and chemical. The former act by replacing oxygen in the air. Such agents are hydrogen, methane, ethylene and nitrous oxide. They are of relatively little importance in industry. The chemical asphyxiants act in either of two ways, preventing the formation of oxyhemoglobin or preventing the utilization of oxygen by the tissues.¹⁵ Carbon monoxide, which inhibits the formation of oxyhemoglobin, has been called "probably the most important industrial poison." This may be the case in other states, but in Massachusetts carbon monoxide ranks far below silica, lead and the organic solvents as an industrial hazard. It is formed wherever organic material is burned in the presence of insufficient oxygen. It has an affinity for hemoglobin three hundred times that of oxygen. Thus when it is inhaled, carbon-monoxide hemoglobin forms in preference to oxyhemoglobin. The usual symptoms seen in all asphyxiation cases are present, namely, tightness across the head, headache, throbbing in the temples, weakness, dizziness, dimness of vision, nausea, vomiting, collapse and coma. The worker should be removed from the contaminated area and given oxygen and carbon dioxide by inhalation.

The chief chemical asphyxiants that prevent the utilization of oxygen by the tissues are hydrocyanic acid and its derivatives—cyanogen, acetonitrile and vinyl cyanide.¹⁶ The last is important, for it is now being extensively used as a solvent in the synthetic-rubber industry. Many of these cyanide compounds can be absorbed through the skin. Treatment of cyanide poisoning consists in the formation of methemoglobin, for cyanide has an affinity for this substance. Methemoglobin can be formed by the administration of sodium nitrite by mouth or by the inhalation of amyl nitrite. Methylene blue in doses of 1 to 2 mg. per kilogram of body weight may be given intravenously for this purpose.⁶

Irritants

The second great group of gases is known as the irritants. These cause inflammation and sometimes necrosis of the tissues with which they come in contact. Some give off a warning odor, but this is not a reliable sign, for the olfactory sense readily becomes fatigued or accustomed to the odor, and so fails to warn of the presence of the irritant. Such irritants include the fumes of acids, ammonia and aldehydes.

Since in general they produce no systemic effects, a few principles will help to keep their action in mind. The first point to be remembered is that the part of the respiratory tract affected varies with the solubility of the inhaled irritant in water; that is, the more soluble the irritant in water, the more readily will it dissolve in the moisture of the upper respiratory tract, with consequent irritation of the nose and trachea. As a result, the worker tends to avoid the area where the fumes are present. The less soluble irritants do not dissolve in the nose and throat, and so penetrate deeper into the bronchopulmonary tree. Since there is less irritation of the nose and the throat, the contaminated area is not avoided and poisoning is apt to ensue. Being only slowly soluble, the effects of these irritants are delayed in onset. Thus eight, twelve or twenty-four hours after exposure, dry cough, tightness of the chest, pulmonary edema, hemoptysis and even death may occur.

The oxides of nitrogen are relatively insoluble gases. Thus the effects of their inhalation are latent, and symptoms do not occur until eight to twelve hours after exposure. Nitrogen oxide fumes are apt to be present wherever nitrates are being used. Nitrates are ingredients of explosives, dyes and plastics and are employed as metal-cleaners.

In contrast to nitrous fumes, chlorine and hydrochloric acid, sulfur dioxide and sulfuric acid are extremely soluble and cause immediate irritating action, mainly restricted to the upper respiratory tract. But chlorine and sulfur dioxide, being gases, also invade the alveolar spaces and so may cause pulmonary edema as well. Other fumes of recent interest are those of the fluorides, now being used as coating agents on welding rods. When such rods are melted, fluoride fumes are evolved, and if these are inhaled in strong concentrations, irritation and ulceration of the upper nasal passages occur, and nosebleed is frequent. Fluorine acts like radium or calcium when it enters the system, and is deposited in the bones in a similar manner.¹⁷ Here it sets up a chronic fibrotic reaction, and a proliferated osteitis occurs. The rate of deposition of fluorine in the bones seems to equal the amount that is being put out in the urine. Ten determinations of fluorides in the urine have been made during the past six months at the Division of Occupational Hygiene. Two of them were over the proposed normal limit of 3 mg. per liter¹⁸; one of the subjects worked in a foundry and the other was a welder.

The last of the irritant gases and vapors to be considered are the aldehydes. Formaldehyde is used in the manufacture of artificial resins and disinfectants. Acrolein is commonly found in proc-

esses where fatty substances are being heated. The aldehydes, being soluble, are extremely irritant to the upper respiratory tract.¹⁰ In high concentrations they are anesthetic.

Metabolic Poisons

Alcohols. Of the aliphatic alcohols, methyl alcohol (wood alcohol) is the most important.²⁰ It is used as a solvent in varnishes, shellacs, lacquers, gums, dyes, rubber cement and plastics, and is employed in dry cleaning. Methyl alcohol, or methanol, unlike other alcohols, is metabolized slowly and so has a cumulative effect. It enters the system principally by inhalation, but poisoning has occurred by ingestion and probably by absorption through the skin. Some people are markedly susceptible to this poison. Exposure to fumes of methyl alcohol causes burning of the eyes, respiratory tract and skin; followed by headache, fatigue, depression, staggering gait, loss of appetite, nausea, vomiting, abdominal pain and diarrhea. In severer cases, cyanosis, confusion, paralysis and visual hallucinations are apt to occur. Methyl alcohol has a specific toxic effect on the optic nerve; any worker who complains of visual disturbance in addition to gastrointestinal symptoms must be questioned closely concerning his occupation.

Other alcohols are not used in industry to any great extent, but in general it can be said that, within certain limits, as the molecular weight increases the narcotic and skin-irritating properties also increase. Thus amyl alcohol, with the exception of methyl alcohol, is the most toxic of the commonly used alcohols. However, since the volatility decreases as the molecular weight increases, there is less chance of exposure to fumes of the higher alcohols; as a result, only a few cases of industrial poisoning from them have occurred.

Chlorinated hydrocarbons. Of the chlorinated hydrocarbons, only four are of interest here.²¹ They are chloroform, carbon tetrachloride, trichlorethylene and tetrachlorethane. The chlorinated hydrocarbons are among the most poisonous of the solvents. They are liver and metabolic poisons and have a marked effect on the nervous system. They cause optic neuritis and atrophy in susceptible subjects, and are also cardiac depressants. In general, the toxicity increases as the molecular weight increases and as the number of chlorine atoms increases.

Carbon tetrachloride has the same structural formula as chloroform, the toxic symptoms of which are well known, except that another chlorine atom has been added.²² This single structural change makes it less anesthetic than chloroform but more toxic to the liver, kidney, heart and brain. It is now little used in industry, but cases of poisoning

from it still occur quite commonly. It may affect the respiratory tract, the gastrointestinal tract, the skin, the liver or the brain. Respiratory symptoms occur when moderate concentrations are inhaled: these include cough, bronchitis, bronchopneumonia, pleuritis, hydrothorax, hemothorax and pulmonary hemorrhage. The gastrointestinal symptoms are anorexia, nausea and vomiting. Carbon tetrachloride is a hyperosmic stimulant; that is, nausea and vomiting may occur without any other toxic symptoms. The liver is often severely inflamed, and there may be yellow atrophy in cases of acute exposure, or cirrhosis in chronic poisoning. Carbon tetrachloride is a depressant and narcotic of the central nervous system. There is often acidosis and a low blood-calcium level in acute poisoning. The acidosis has been ascribed to the absorption of hydrochloric acid, but it may be due to disturbance of the oxidative function of the liver.

Trichlorethylene,²³ the third important chlorinated hydrocarbon, is an unsaturated compound that is noninflammable and a relatively good solvent. It is less irritating to the respiratory tract, less injurious to the liver and less narcotic than most of the other chlorinated hydrocarbons. In low concentrations it creates a pleasant feeling of intoxication, with unsteadiness, confusion, mental dullness, anorexia, nausea, vomiting and fatigue. Constant exposure has led to the development of addiction and has caused retrobulbar neuritis and polyneuritis. In high concentrations this substance is narcotic.

Tetrachlorethane²³ is the only other halogenated saturated hydrocarbon of importance. It is used in lacquers and varnishes. Having a high molecular weight and four chlorine atoms, it may be expected to have marked toxic properties. As a matter of fact, it is probably the most poisonous of the chlorinated hydrocarbons, possessing severe narcotic properties and causing acute yellow atrophy of the liver and a fatty change in the heart and pancreas.

Other organic substances. There are a few other organic substances in use that are rapidly becoming of increasing importance.

One of these is methyl ethyl ketone (butanone).²⁴ The recent development of synthetic methods of preparation has made it available in commercial quantities, and it is being used in lacquers, cements, varnishes and paint removers and in the manufacture of drugs. It is an irritant to the conjunctiva and nasal mucosa, but as yet no cases of industrial poisoning from it have occurred. In high concentrations it will probably prove to be a pulmonary irritant and a narcotic.

The glycols are aliphatic hydrocarbons with two hydroxyl groups. They are good solvents and are of low volatility. In general, they are narcotic if

inhaled in high concentration. They cause serious kidney damage if ingested.

The cellosolves are ethers that are derived from the glycols.²⁵ They also contain an alcohol radical and retain many of the characteristics of ethers and alcohols. They are irritants and depressants of the central nervous system. They are excellent solvents for cellulose, natural resins, acetate lacquers and enamels. Chronic exposure causes headache, dizziness, stomach disorders, psychotic symptoms, mental retardation and polyneuritis. Anemia, thrombocytopenia and granulocytopenia have been reported from exposure to these solvents.

Aromatic compounds. Last come the aromatic compounds, comprising benzene and its derivatives.^{15, 21} Benzene is an excellent solvent for rubber, cellulose, gums, resins, fats and oils, and is used as an ingredient of many paint removers. It is an anesthetic and is a depressant to all the elements of the bone marrow. Chronic exposure causes anemia, leukopenia and thrombocytopenia. Benzene poisoning can be suspected when the white-cell count is persistently under 5000 and the red-cell count under 4,000,000 in a person exposed to benzene vapors. Change in the urine sulfate partition is one of the best diagnostic criteria for benzene exposure.²⁶ Normally 90 per cent of the urine sulfate is in inorganic form and 10 per cent ethereal. After exposure to benzene, the percentage of ethereal sulfate tends to increase. When it becomes 50 per cent of the total, benzol poisoning can be suspected.

The introduction of methyl groups to the benzene ring gives toluene and xylene. There is no unanimity of opinion regarding the toxicity of these substances, but it is generally thought that they are more narcotic but less hemotoxic than benzol. In any event, they are less apt to be found in toxic concentrations in industrial plants, and so have been recommended as solvents in place of benzol for many purposes.

By the introduction of an amino group into the benzene ring, aniline is formed. It is used as an intermediate in the manufacture of drugs, dyes, resins, inks and rubber accelerators. Aniline and its immediate homologues affect the blood and the central nervous system. The main portal of entry is by way of the skin, and only a few cases of poisoning have occurred by inhalation. In acute poisoning, one sees weakness, somnolence, headache, vertigo, convulsions and even death.²⁷ In chronic poisoning, the most striking effect is on the blood. There is hemolysis of the red cells, as well as the formation of methemoglobin. Cyanosis is commonly seen in workers with aniline. The white cells ordinarily show little change, but there may

be depression of all the bone-marrow elements, as in benzene poisoning. Bladder tumors have been reported.

The toxicity of the aminobenzenes can be best remembered by recalling that the sulfonamides are among them. Acetanilid is another aniline derivative. These drugs cause confusion, loss of appetite, nausea, vomiting, methemoglobin formation and many other well-known toxic signs and symptoms. It is therefore unnecessary to memorize the symptoms and signs of aniline poisoning, for the picture is similar to that seen in poisoning from the sulfonamides and the antipyrine group of drugs.

The nitrobenzenes are also hemolytic poisons and depressants of the central nervous system.²³ Like aniline, they can be absorbed through the skin. They are extensively used in the manufacture of explosives.

Trinitrotoluene, one of the nitrated aromatic compounds, is also absorbed through the skin. It has been reported to have caused cyanosis, methemoglobinemia, chronic gastritis, anemia and jaundice. It causes yellow discoloration of the skin hair and nails and is a skin irritant.

The chlorobenzenes are extensively used in moth balls and also in anti-moth sprays for fur and other clothing. The chlorobenzenes are probably more narcotic than benzene but less hemotoxic. Jaundice, kidney damage and methemoglobinemia have been reported from exposure to them. Since some of the chlorobenzenes are solids, one should inquire concerning the solvent used in commercial liquid preparations; chloroform, carbon tetrachloride, benzol and carbon disulfide are frequently employed and are toxic in their own right.

* * *

This concludes the discussion of the common toxic dusts, fumes and gases encountered in industrial practice. With the increasing employment of inexperienced young and old workers, it is imperative that all physicians be on the alert for illness due to industrial exposure, for only by the early diagnosis of such illness can the men at the front lines be supplied with the necessities of an airtight war.

23 Joy Street

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THE CONDITIONED REFLEX AS A TREATMENT FOR ABNORMAL DRINKING

Its Principle, Technique and Success

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NO OTHER disease is so widely spread or so detrimental from the medical, sociologic, legal, economic or any other point of view as is chronic alcoholism. The experience that will power and good intentions on the part of the unfortunate alcoholic patient are in most cases as inefficient as a pledge led physicians, and especially psychiatrists, to look for another, more promising cure. Unfortunately, all the usual types of therapy—hospitalization (voluntary or by commitment), "alcoholic farms," sedation, vitamins, gold injections, amphetamine (Benzedrine) and even psychotherapy, inclusive of psychoanalysis—have proved to be of help in not more than 15 to 25 per cent of the cases so treated. A proportion of cures of 50 to 75 per cent claimed for any form of therapy can easily be reduced to a more accurate figure by asking what period of total abstinence without relapses is meant by "cure," and how many records of patients can be produced.

Everyone is familiar with the fact that the ingestion of tainted food causes sickness, disgust and abhorrence for this kind of food for a long time. The sight, smell, taste or even thought of it makes one sick. Moreover, the inability to take good, untainted food resembling it in appearance, smell or taste may last for weeks, months or years. A physiologist would describe the mechanism of this phenomenon thus:

Clostridium botulinum is the unconditioned stimulus causing the unconditioned reflex response of sickness and vomiting. The meat or fish is the conditioned stimulus that is able to elicit later the conditioned reflex of vomiting even after omission of its real, original cause.

By substituting for the toxin (unconditioned stimulus) an emetic and for meat (conditioned stimulus) an alcoholic beverage, more or less at the same time there will be developed, after a period of treating or conditioning, the conditioned reflex of emesis whenever alcohol is seen, smelled or tasted. Simple as this principle sounds, it is difficult or impossible to accomplish the desired results without knowledge of all the peculiar characteristics of a conditioned reflex. That is why so many attempted forms of treatment based on this idea have been unsuccessful.

The earliest scientific attempt at treating alcoholic patients by using an emetic as an unconditioned stimulus was made in 1933 by two Russian physicians, Sluchevsky and Friken.¹ The emetic used by them was apomorphine. Seven patients were treated. On only one of them, however, were continued observations made. This patient was reported as having developed the conditioned reflex several weeks after the treatment was completed. Several therapists reported subsequently on apomorphine as the unconditioned stimulus. The number of patients in all cases was small, the largest group being 36, mentioned by Fleming,² who estimated 25 per cent of perma-

*The toxic product of protein decomposition, ptomaine, or the exotoxin produced by *Clostridium*

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nent cures. He thought, however, that the sincere co-operation of the patient was essential for success, and that almost any method of treatment would be successful with this type of patient.

There is an old treatment with a familiar name that is based on the right principle. However, it fails because of a faulty technic. In it, the emetic is added to the alcoholic drink. The alcohol is soon absorbed and the patient is partly intoxicated—that is, narcotized—at the time when the emetic acts. Pavlov proved that no conditioned reflex can develop in a narcotized subject. Further, the emetic used in this cure has two bad complementary aftereffects: a euphoric and a hypnotic one. The result of the euphoric state is that the patient, instead of feeling sick after the treatment, feels "fine," which does not promote development of the reflex of abhorrence and nausea. The hypnotic aftereffect causes a sound sleep for several hours, with subsequent amnesia, which also is not conducive to the desired results.

Finally, however, after years of research and experimentation, the right kind of emetic (emetine), with all the desired properties and none of the disturbing ones, was selected and a careful and skilful technic was devised. Voegtlin and Lemere³⁻⁵ have practiced this treatment for six years. They use a solution of 50 gr. of emetine (an alkaloid of ipecac), 25 gr. of pilocarpine and 23 gr. of ephedrine in 40 cc. of water, 0.4 to 1.0 cc. of which is injected intramuscularly 4 to 12 minutes before a drink is given to the patient. In accurate follow-up reports on 1194 patients they give the following results⁶: 74.8 per cent of 644 patients treated for less than two years were still abstinent; 52.5 per cent of 291 patients treated from two to four years ago were still abstinent; and 51.5 per cent of 259 patients treated four or more years ago were still abstinent.

For successful conditioned-reflex therapy, all extraneous auditory, olfactory and visual stimuli must be eliminated and the conditioned stimuli emphasized.

The elimination of auditory extraneous stimuli is achieved by a soundproof treatment room and by avoiding conversation during treatment. The positive auditory stimuli are purposely exaggerated—the clinking of bottles and glasses, the gurgling sound of liquor being poured into glasses and the sounds of retching and vomiting.

Undesirable visual stimuli are all furniture and articles in the treatment room that are not essential for the treatment. The room should be painted a plain dull color and contain a comfortable chair for the patient and another for the therapist, and a bar or table with liquor bottles and glasses on the spotlighted surface.

Sundry medical supplies (syringe, emetic solution and so forth) should be on a shelf of the bar or table invisible to the patient.

Olfactory stimuli that may vitiate the treatment are odors arising from the kitchen, laboratory, medicine chest (paraldehyde) or lavatory. Conditioning olfactory stimuli are emphasized by having the patient smell of the glass before and after the drinking. As the pilocarpine used in the emetic increases the secretion of nasal mucus, the patient should be reminded to blow his nose frequently.

No food and no sedatives should be given within twelve hours before treatment. Any narcotizing agent (alcohol, barbiturates, bromides, chloral hydrate and so forth) taken after the treatment counteracts the conditioning; stimulants like amphetamine (Benzedrine) further it.

The treatment sessions are given four to seven times on successive days and repeated once after one, two, three, six, nine and twelve months during the first year.

It is well to keep in mind that the treatment should be used in common with psychotherapy and social therapy in order to eliminate the extrinsic and intrinsic factors that cause or contribute to drinking.

The results of the treatment depend largely on the selection of patients suited to this type of therapy; patients with psychopathic traits and those whose attitude lacks sincerity and co-operation are apt to be failures.

Conditioned-reflex therapy as practiced at the Washingtonian Hospital differs from the treatment employed by Voegtlin and Lemere in the formula of the emetic solution used and in the after-therapy. It was found that when pilocarpine and ephedrine were given in the amounts used in their treatment, the patients developed spasms of the urinary bladder and intestinal tract. This not only was painful, but because the treatment had to be interrupted to relieve the spasm, the mind of the patient was diverted and the conditioned-reflex therapy was thereby lessened in effect. Furthermore, probably owing to the large amount of pilocarpine used, the patient complained of blurred vision of sufficiently severe degree to make it difficult for him to read even the labels on the bottles on the treatment table. This produced in him fear of definite visual damage and again his mind was diverted from the treatment. On the other hand, the dosage of ephedrine was not sufficiently high to prevent the drop in blood pressure that emetine usually provokes. It was found that the systolic blood pressure of the majority of patients, measured the morning before treatment, is 100 or less. When emetine was superimposed on the

customary low blood pressure in the majority of chronic alcoholic patients may cause dangerous shock. For these reasons the amount of pilocarpine in the stock solution was reduced to 15 gr. and that of ephedrine increased to 30 gr. It was also found that if ephedrine was given an hour before the treatment, sometimes the effects wore off and the blood pressure fell, owing to the combined effects of the emetine and the lapse of time. For this reason it proved preferable to increase the amount of ephedrine in the solution given, rather than to administer it beforehand.

The after-therapy practiced in this hospital varies from the Voegtlin and Lemere treatment in the following particular. It is believed that psychotherapy, carried out on the traditional intellectual level and, even more important and efficacious, on the emotional level, is of great value as an adjunct to drug therapy. It was found insufficient for the patient to return at intervals of one, two, three, six, nine and twelve months for reinforcement therapy. Contact with the hospital and with the physician is inadequately maintained unless the patient sees the doctor and returns to the hospital environment at regular weekly intervals. Only by coming back frequently is the bond between the patient and the physician strengthened and the psychologic impression of both the physical and the psychical strain accompanying the conditioned-reflex treatment maintained. By supplementing the monthly periods of reinforcement by weekly visits, the patient is prevented from slipping into the delusion of the conviction that he can take a social drink without relapsing. By frequent visits, moreover, he is kept in the mental attitude of a

patient still under treatment. His approach to the reinforcement therapy thus has less psychic shock and he dreads the treatments less than would be the case if a month or more had gone by before he came to the hospital again. The patient is therefore urged to spend his week ends and other free time within the hospital for a period of several weeks and, if possible, months, in addition to returning for reinforcement treatments.

Although conditioned-reflex therapy, employing the technic described, has been in operation in this hospital for too short a period (seven months) for the results to be conclusive, the number of successful treatments is extremely gratifying. Of 43 patients treated, 27, or 63 per cent, have been entirely abstinent since treatment, which represents the longest period in their lives of freedom from drinking. It is thought that this figure shows that the treatment has been efficacious and is worthy of further trial.

SUMMARY

The use of the conditioned reflex in the treatment of chronic alcoholism is discussed, and its apparent success in a small series of cases is described.

41 Waltham Street

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CLINICAL NOTE

VARICELLA FOLLOWING EXPOSURE TO HERPES ZOSTER

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VON BOKAY,¹ in Budapest in 1892, first made note of an apparent relation between herpes zoster and varicella; he² reported further cases in 1909. Since that time the clinical relation between the two diseases has been repeatedly, even if not frequently, noted.

Among the more recent reports is that of Blatt, Zeldes and Stein,² who in 1940 published 2 case histories from the Children's Division of the Cook County Hospital. In the first, a bedridden child in the tuberculosis ward developed herpes zoster eleven weeks after admission. Thirteen days later a contact who had had no other exposure for a year developed varicella, and thirteen days later a third child developed varicella after exposure to the second child. In the second case two children developed varicella fourteen and eighteen days after exposure to a nurse with herpes zoster. This nurse had previously had chicken pox. It is of interest that no generalized epidemic followed either of these incidents.

Weigand,³ in 1942, reported two siblings who developed typical chicken pox two weeks and four weeks respectively after exposure to a grandmother suffering from herpes zoster. Presumably the second child, with a severer infection, developed the disease as a result of contact with the first. There had been no other exposures.

In the interest of adding further presumptive evidence of an infectious phenomenon not commonly seen and not as yet universally accepted to that already accumulated, the following cases deserve brief mention.

The mother of two children, a daughter, aged 8, and a son, aged 6, first noticed soreness of the left side of her throat on January 23. By January 28 pain and swelling of the left side of the face had developed, and on January 30 a typical eruption of herpes zoster appeared in this area. She had had varicella in childhood. Fourteen days after her first symptoms had appeared, the son showed the scattered papules of an eruption that became well-defined varicella 24 hours later, and on the following day the husband and the daughter broke out with typical, moderately severe chicken pox. No known exposure to chicken pox had occurred for any of the three. The daughter had been confined to the house with a cold since the beginning of her mother's illness, and no cases had occurred in the small school group of which the son was a member.

The literature on the zoster-varicella relation was reviewed by Bruusgaard⁴ in 1932, and by Blatt, Zeldes and Stein² in 1940. As a result of the lack of exact knowledge about so many of the aspects of virus infections, there continue to exist two schools of thought concerning their relation. The dualists, represented chiefly by Comby,⁵ believe in two separate and distinct viruses as the etiologic agents of the two diseases. The monists, including von Bokay,¹ Netter and Urbain,^{6,7} Lipschutz and Kundratitz,⁸ Kundratitz,⁹ Bruusgaard⁴ and others, believe that the two infections are caused by the same virus with the faculty of undergoing mutation in regard to infectivity and tissue affinity, changing from a neurotropic form in herpes zoster to a dermatotropic form in varicella. Goldsmith¹⁰ is responsible for the statement that persons develop varicella following exposure to herpes zoster ten times more frequently than do those following exposure to varicella.

The arguments of the dualists are based on the differences between epidemiologic and immunobiologic conditions obtaining in the two diseases. Varicella, for instance, leaves a pronounced immunity, whereas not infrequently patients who have had varicella later develop herpes zoster. Varicella is a disease of childhood, whereas herpes zoster rarely attacks children, its highest incidence being in the sixth decade. Varicella is highly communicable, but herpes zoster is only slightly so. Cantor,¹¹ moreover, in twenty years on a Pacific island saw much herpes but no varicella, whereas Støren¹² had a similar experience in Norway.

The theory of monism is based not only on the clinical evidence supplied by cases of varicella apparently resulting from exposure to herpes zoster, but on considerable experimental work as well. Thus various investigators, notably Netter and Urbain,^{6,7} have demonstrated by complement-fixation tests that serums of patients with these diseases contain identical antibodies. This, of course, may be only the expression of a group reaction between closely related although nonidentical viruses, but it is a challenging observation.

It is of interest that the same complement fixation occurs with so-called "symptomatic" herpes zoster, such as that sometimes appearing after the introduction of arsenic or bismuth, or following smallpox vaccination. In these cases the reaction is probably due to the activation of a latent virus by factors acting as *agents provocateurs*. This is consistent with the property of latency apparently possessed by the viruses of herpes, both zoster and simplex.

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Inoculation with the fluid from zoster vesicles has been reported by Lipschutz and Kundratitz⁸ and by Bruusgaard.⁴ Lipschutz and Kundratitz found that some subjects developed only local reactions, and some a generalized varicelliform eruption as well. Children who had recovered from varicella were immune to zoster inoculation (although not necessarily immune to herpes zoster in adult life), and children who had recovered from natural or experimental herpes zoster were immune to inoculation with varicella fluid; moreover, serum from subjects convalescing from herpes zoster could be used as a protection against varicella.

Examining tissues histologically, Bruusgaard found that the varicella-like lesions resulting from inoculation with herpes zoster fluid show the same microscopic picture as that of the vesicles from ordinary herpes zoster or varicella, accompanied by degeneration of the epithelial cells with vacuolation and oxyphile elements in the nuclei, and multinucleated cells.

Bruusgaard's own cases comprise five series, each series having been inoculated from a different case of herpes zoster. Eight out of a total of 18 children showed positive takes seven to nine days later. In 4 of these there was only a reaction at the site of the inoculation. In the other 4 cases a generalized exanthem indistinguishable from varicella appeared fourteen days after inoculation, in addition to the local reaction. All positive results were in children under five years of age. A considerable number of secondary cases of varicella, all comparatively mild, occurred among children exposed to the inoculated group.

It is apparent that the proponents of the theory of a single, mutable virus for herpes zoster and varicella can present strong evidence to support their claims, even if exact proof is lacking. Thus the generalized eruption of herpes generalisatus, indistinguishable from varicella, assumes special interest as the best evidence available that the neurotropic virus of herpes zoster may also show definite dermatotropism.

Zinsser,¹³ in developing the thesis that many examples exist in nature in which modifications of

virus seem to have developed spontaneously, points to the relation between herpes zoster and chicken pox as a likely one, and Sabin,¹⁴ discussing the neurotropic virus diseases of man, alludes to the strong possibility that herpes zoster and varicella may be manifestations of the same virus.

As Bruusgaard concludes:

The same difficulties arise here as are encountered in the interpretation of the reciprocal relations between the different types of other ultramicroscopic viruses, to meet which difficulties we try in the meantime to seek assistance from speculation and theories. The reasons for this, as Doerr emphasizes, are sufficiently clear, namely, the fact that none of these infective substances have been identified morphologically, and that they have not proved culturable in the laboratory.

SUMMARY

Three cases of varicella following exposure to a case of herpes zoster are reported, and the relation between varicella and herpes zoster is discussed.

266 Beacon Street

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MEDICAL PROGRESS

RECENT ADVANCES IN TESTOSTERONE THERAPY*

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MUCH has been learned of the effects and therapeutic usefulness of testosterone since the previous review on this subject by one of us (J. C. A.) in 1940. Newer concepts of its physiology and wider clinical experience warrant, perhaps, another summary of the knowledge concerning this important endocrine substance.

Physiology

The history of the discovery and isolation of the male hormone has recently been well summarized.² Testosterone, first synthesized by Ruzicka and his associates,³ in 1935, is apparently identical with the hormone of the interstitial cells of the testicle. Its most striking effects, manifested naturally in the normal adolescent male or artificially by the administration of the hormone to patients with testicular deficiency, are already well known. They consist of a development of secondary sex characteristics, and a growth of the penis, scrotum, prostate and seminal vesicles; the appearance of hair on the pubis, face and other areas of the body; a deepening of the voice; and a development of the masculine behavior patterns of aggressiveness, vigor and self-confidence.

The relation of testosterone to the various endocrine organs is in need of further clarification. Like the secretions of the other peripheral endocrine glands, testosterone appears to exert a specific inhibitory action on the pituitary gland.⁴⁻⁶ In females and eunuchoid males treated with testosterone, there is a decrease in the excretion of the gonadotropic hormone of the pituitary.⁷⁻⁹ In studies on women it was found that the administration of testosterone inhibits follicle formation, ovulation and the formation of the corpus luteum in the ovary, probably through its effect on the hypophysis.⁵ These effects occur with large doses of the drug, but smaller amounts of testosterone exert a stimulating effect on the adrenal, thyroid and parathyroid glands and on the ovary as indicated

in animal experiments.¹⁰ It appears to be a not unusual occurrence that small amounts of the target glands stimulate whereas larger amounts inhibit the anterior pituitary gland.

Recent investigation has increased appreciation of the role that testosterone plays in the metabolism of the body as a whole. Many have observed an increased basal metabolic rate under the influence of testosterone,¹¹⁻¹⁶ and one group¹⁵ by showing a lowering of the respiratory quotients suggests that it may effect a greater oxidation of fats. Like other steroid hormones, testosterone has been observed to cause a decreased excretion of electrolytes and water.^{15, 17, 18} A definite retention of phosphorus and nitrogen occurs during its administration,^{12, 15-20} and to a greater degree than can be explained by the genital hypertrophy. This is taken to be an indication of a generalized increase in musculature, a view that is further strengthened by the finding of increased excretion of creatine in treated patients^{20, 21} or paralleling a rise in urinary androgen in children.²² Patients with hypogonadism treated with androgens also exhibit a marked increase in endurance and the ability to perform static and dynamic work,^{23, 24} although this effect is not produced in normal men.²¹ This is of interest inasmuch as it goes far to explain the greater musculature of the males of most species, particularly strikingly shown in the male deer during the season of testicular hypertrophy and activity. These findings of the important role that testosterone plays in nitrogen metabolism and growth of muscle and bone form one of the most promising developments of recent endocrine investigation. Their therapeutic implications have already been realized in the treatment of retarded growth, but more widespread usefulness should certainly be discovered in the near future. An unexplained lowering of glucose tolerance and a decrease in liver glycogen have been reported during the administration of methyl testosterone.^{11, 13}

Any clinician who has observed the delicate, light skin and the vasomotor instability of eunuchoid patients has been impressed with the importance of testosterone to the skin and vascular system. These clinical impressions are confirmed by studies that show a decreased excitability²⁵ and an increased velocity of blood flow¹⁵ in vessels after testosterone administration. An increased

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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permeability of the capillaries in the rat uterus and vagina has been reported.²⁶ The possibility that the sex hormones and the androgen : estrogen ratio are related to the occurrence of acne vulgaris has been discussed,^{27, 28} although their mechanism is still to be understood. The predominant occurrence of this disease in adolescent boys and the good reports with estrogens as therapy²⁹ suggest that relative increase of testicular secretion plays some part. This is confirmed by the not infrequent appearance of acne in eunuchs treated with testosterone. It is not certain that this reaction is dependent on the androgen : estrogen ratio, but it must be recalled that boys and girls excrete both 17-ketosteroids and estrogens, with only a variation in quantity to differentiate the sexes.³⁰ An interesting property of testosterone is its ability to produce a significant increase in red cells and hemoglobin in eunuchoid individuals.^{33, 31}

Methods of Administration

Few substances equal testosterone in the variety of routes whereby it may be effectively administered. The classic route—by intramuscular injection in the form of testosterone propionate in oil—still has much to recommend it. Its effects are rapid and sufficiently sustained to require only two or three injections per week. It was soon found, however, that testosterone and its derivatives, like some other steroid hormones, are absorbed through the skin, and many have advocated their administration by inunction.³²⁻³⁵ Although the dose required compares favorably with that of intramuscular injection, the type of base used has a great deal to do with the effectiveness of absorption.³⁶ In our experience this type of therapy has not been extremely successful, and neither generalized nor local effects have been spectacular.

In an attempt to effect a slow and physiologic absorption of this hormone with a minimum of inconvenience, some have used the technic of subcutaneous implantation of sterile pellets of testosterone and its derivatives, such as the propionate.^{31, 37-41} Studies of the absorption rates of such pellets demonstrate that both testosterone and the propionate ester are relatively well absorbed.^{42, 43} This confirms the clinical impression that effects may be exerted for periods of weeks to several months. Although this technic is far more economical with respect to the necessary quantity of the hormone, it has been deemed unsatisfactory by some,^{44, 45} and others have found that the implants occasionally slough⁴⁶ or become infected.⁴¹ On the whole, however, this technic has been recommended as easier than continuous injections, and some prefer it to the ingestion of tablets. It

has the advantage of a constant, rather slow, absorption rate.

The recent development of methyl testosterone offers a form of the drug that is clinically effective when taken by mouth. Except for a few dissenting voices,⁴⁵ investigators are agreed on the efficacy of this form of administration.^{14, 23, 33, 34, 40, 47-50} In our experience it works particularly well in stimulating body growth and development. There are apparently no side effects except for occasional mild gastric distress, easily relieved by alkalis. This drug is said to cause less hirsutism in the female, though we have certainly seen it develop; it produces all the other anatomic changes produced by testosterone parenterally. The only objections to the oral use of methyl testosterone are its comparative expense, since considerably more than the parenteral dosage is required, and the fact that its effects develop somewhat less rapidly. The sublingual route has been used successfully for the administration of testosterone and its derivatives.⁵¹

Indications

Diseases peculiar to males. In this group of diseases one finds the most physiologic and rational indications for testosterone therapy. Favorable and usually dramatic results are achieved with replacement therapy in all types of *adult testicular failure*.^{40, 41, 50, 52-56} Beneficial effects become evident in the first week and improvement continues during treatment. Infantile genitalia enlarge except for the testes, erections and ejaculations occur, the growth of masculine hair is stimulated, and eventually a beard may develop. Increase in virility is reflected in changes in body contour, enlargement of the larynx with a deepening of the voice, and changes in the skin and musculature. Either as a direct result of the hormone or indirectly by virtue of the encouraging changes, the emotional status improves, and there is increased confidence and aggressiveness and greater emotional stability. There is reason to mention, however, the opinion of Pullen and his co-workers⁵² that before employing substitution therapy in this condition an accurate diagnosis should be established; he even suggests that a preliminary trial of pituitary gonadotropic hormone be made. Despite favorable results with testosterone in *delayed puberty*,^{57, 58} Hamilton⁵⁹ has made the warranted suggestion that such treatment is unwise. He believes that substitution therapy can well wait a few years until it is obvious that testicular function will not begin naturally. This suggestion has merit, for testosterone stimulates only secondary sex characteristics, having no effect on the development of the testicle or of spermatozoa. In fact, in large doses it may inhibit such development. In

cryptorchidism, testosterone alone or combined with gonadotropic hormones has enjoyed some success,^{57, 58, 60} and probably deserves a trial before surgical intervention. Likewise, in *benign prostatic hypertrophy* some reports on the use of testosterone are favorable,⁶¹⁻⁶⁴ although one group⁶⁴ found no improvement in urinary symptoms. In view of the finding of decreased androgen excretion in cases with prostatic hypertrophy,^{65, 66} the use of testosterone in this condition is not irrational, and it is possible that it might be of value in early cases and poor operative risks. Further confirmation of this viewpoint appears to be needed. The use of testosterone in *male sterility* appears to us to be questionable,^{67, 68} although in one reported case of sterility associated with hypogonadism there was an increase in the number and motility of spermatozoa and two pregnancies apparently resulted from its use.⁴⁶ Most reports on the effect of testosterone in *functional impotence* are discouraging,^{46, 56, 69-71} but a favorable result has been reported with testosterone and gonadotropin combined.⁷²

Gynecologic conditions. In a wide variety of diseases peculiar to women, the male hormone has found useful clinical application. In *mastodynia* its use has met with success,^{45, 73-75} and Nathanson⁷³ has found it more effective than the estrogens. *Postpartum engorgement of the breasts* responds well to testosterone,^{74, 76-78} but dosage should be moderate (8 mg. daily by injection or 60 mg. of methyl testosterone by mouth for two days, beginning on the second to the fourth postpartum day). Abarbanel⁷⁹ finds that moderate dosage does not suppress lactation. One group⁸⁰ found testosterone of little or no value in this condition, but they employed small doses of testosterone propionate. To achieve *inhibition of lactation* some have found testosterone useful in large doses (75 mg. intramuscularly, 90 mg. of methyl testosterone orally per day).^{74, 77, 81}

Those who have used the male sex hormone in the treatment of *functional uterine bleeding* have secured very favorable results that in many cases persist after the treatment is discontinued.^{44, 45, 74, 82-85} Temporary regression in the size of *uterine fibroids* has been observed.^{30, 84, 86} Encouraging results have been reported with the use of testosterone or methyl testosterone for symptoms of the *menopause*,^{45, 74, 75} and in some individuals we have found it more effective than the estrogens. Moderate doses of testosterone given for two weeks preceding menstruation are reported to relieve *premenstrual tension*^{35, 74} and certain cases of *functional dysmenorrhea*.^{35, 45, 74, 75} Beneficial effects have been reported with the androgens in a host of other gynecologic conditions in-

cluding *afterpains*,⁷⁴ *pelvic inflammatory disease*,⁸¹ *nocturia* from various causes⁸⁸ and *nymphomania*.⁸⁹ In an experimental study of a case of *endometriosis*,⁹⁰ the symptoms were controlled by large doses of testosterone but with the production of disagreeable side effects.

General diseases. Testosterone, like most new drugs, has been tried in a variety of conditions, not always on the soundest physiologic basis. Many such trials have given surprisingly favorable results. In view of the widespread physiologic effects of testosterone, which have been discussed in an earlier part of this paper, it is perfectly possible that the male sex hormone may exert a beneficial action on systems other than the urogenital tract.

Testosterone, alone or combined with gonadotropins, has been used and is recommended in cases of *retarded growth*,^{46, 91-93} where it produces marked increases in growth rate and bone development.^{19, 91, 94} Conversely, it has been reported to be useful in arresting *abnormally rapid growth*.^{92, 95} In our experience with a large number of adolescents with retarded growth the effect of prolonged use of methyl testosterone has been striking, indeed far better than that achieved with any other therapy. Although the response is more marked in the first six months of therapy, there continues to be a satisfactory growth for many months thereafter. To achieve these effects, however, it is essential that the bone epiphyses be open. It is not surprising, perhaps, that better results are obtained in children who have not an inheritance of small stature.

In a host of psychoses, testosterone compounds have been used with varying degrees of success. Cases of *agitated depression*⁹⁶ and *atypical involutional psychoses*⁹⁷ have responded encouragingly to testosterone. Both good and poor results have been obtained with testosterone in *male involutional psychoses*.^{98, 99} One patient with *schizophrenia associated with hypogonadism* made a striking recovery with androgens,¹⁰⁰ but the physical abnormalities may have had a major share in the patient's mental derangement. In the same manner, *behavior problems in adolescence* when associated with hypogonadal states tend to disappear after the physical inferiority has been improved with testosterone.⁵⁸ Because of the frequent remissions and relapses that may occur spontaneously in most psychoses, one must await better controlled studies, larger series of cases and longer periods of observation before venturing to appraise this aspect of testosterone therapy.

Various *dermatitides associated with senescence* in males have responded to androgen therapy after other treatment had failed.¹⁰¹ An interesting ap-

plication of testosterone is its recent use in certain disorders of the vascular system. In *essential hypertension* and *peripheral vascular disease*¹⁰² sufficient improvement has been reported to warrant further investigation.¹⁰² Lesser,¹⁰³ Bonnell and others,¹⁰⁴ Hamm¹⁰⁵ and Walker¹⁰² all report good results in the treatment of *angina pectoris* with testosterone, although such treatment did not prevent the occurrence of a coronary occlusion in one patient.¹⁰²

Two patients with *myotonia atrophica*, associated with testicular atrophy, responded markedly to testosterone treatment, whereas a patient with no testicular involvement did not improve.¹⁰⁶

Possible Harmful Effects

The conscientious physician before employing a new drug wants to be informed of the deleterious effects that may attend its use. Permanent harm resulting from the moderate use of testosterone remains to be demonstrated. It must be remembered, however, that the synthetic androgens are comparatively new and have had only a limited clinical trial.

Some have warned against the use of testosterone in growing persons on the ground that it may cause premature epiphyseal union and consequent dwarfing.¹⁰⁷ Pullen and his group⁵² found no advance in bone age in children who received 30 mg. of testosterone propionate weekly, although when 75 mg. was administered per week such changes did occur. Others in fairly large series found no evidence of epiphyseal closure or advance in bone age.^{57, 91, 94}

Moore¹⁰⁸ has stated that the administration of androgens to males with normal testicles may be harmful; and indeed, decreases in number of spermatozoa and in ejaculation volume have been noted.^{50, 107, 109} Such observations emphasize the need for a definite diagnosis of diminished testicular function before employing substitution therapy in the form of testosterone and condemn its indiscriminate use in normal man. Eidelsberg and Ornstein¹¹⁰ have shown that in eunuchoid males testosterone treatment may be employed over long periods of time without ill effect. Gynecomastia has occasionally been observed in males during testosterone therapy,^{50, 59} but in our experience this effect is only transient and disappears with reduction or elimination of the drug.

In females receiving androgenic therapy, the commonest untoward effects are the appearance of hirsutism, deepening of the voice and hypertrophy of the clitoris,^{45, 67, 75, 83, 84, 80, 90, 111} The change in voice remains, though these other effects are transient and regress if treatment is immediately stopped. It is occasionally noted that the increased hirsutism remains after discontinuing the drug,

but this is not easy to evaluate. Moreover, with dosage below 250 mg. of testosterone propionate per month, such effects are extremely unlikely.⁸² Acne,⁸⁴ weight gain⁸⁴ and increased libido⁴⁵ are occasional and transitory side effects in women. Increased libido may be marked in castrated women. Wollner¹¹² has reported a proliferative change in the cervical mucosa resembling carcinoma in a patient with chronic cervicitis who received fairly large doses of testosterone propionate.

Dosage

With so many effective routes of administration available to the physician, each with its advantages and drawbacks, it is difficult to recommend one above another. Dosage and form of administration will vary depending on the economic status of the patient, age and sex, and the condition that is being treated. A standard treatment regimen may, however, be suggested, to be changed in accordance with individual factors. It might consist of intramuscular injection of testosterone propionate in doses of 20 to 25 mg. three times weekly until the desired effects are produced, then substitution of maintenance doses of 10 to 40 mg. daily of methyl testosterone by mouth. Children should not receive more than half the adult dose, and in the case of women it is well to keep below a total of 300 mg. per month in order to avoid the masculinizing effects that are good evidence for reducing the amount of the drug. Where different dosage has been suggested for specific conditions, we have endeavored to include it in the discussion.

SUMMARY

Testosterone is a synthetic and as yet fairly expensive product identical with a testicular hormone. Its most dramatic therapeutic effects are seen when it is used in the form of physiologic replacement therapy in true testicular failure, but it has been shown to have beneficial effects in other diseases. Its evaluation in many of these conditions must await further investigation. There is as yet no evidence of permanent harm resulting from its moderate and clearly indicated usage.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Stated Meeting, February 3, 1943

A STATED meeting of the Council of the Massachusetts Medical Society was called to order by the president, Dr. George Leonard Schadt, at 10.30 a m, on Wednesday, February 3, 1943, in John Ware Hall, 8 Fenway, Boston; 175 councilors (Appendix No 1) were present

The Secretary offered the record of the meeting held October 7, 1942, as published in the *New England Journal of Medicine*, issue of November 12, 1942, and moved its adoption. This motion was seconded by Dr. Peirce H. Leavitt, Plymouth, and it was so ordered by vote of the Council.

The report of the Auditing Committee for the year ending December 31, 1941 (Appendix No. 2) was presented by Dr. LeRoy A. Schall, West Newton, chairman. Dr. Schall explained that this report was not offered in February, 1942, because the accountant's report had not been received sufficiently early to make this possible.

He spoke of having approached the Treasurer with a view of learning what the duties of the Auditing Committee were. He quoted the latter as having said that it was not necessary for the Auditing Committee to appear before the Council. A statement signed by the committee and addressed to the Council, to the effect that the latter had examined the accountant's report, was all that was necessary. Dr. Schall moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

The report of the Auditing Committee for the year ending December 31, 1942 (Appendix No. 3), was presented by Dr. Burton E. Hamilton, Brookline, in the absence of Dr. Francis C. Hall, Brookline, chairman.

The report spoke of the duty of the Auditing Committee to require the examination by a certified public accountant of the assets and liabilities of the Society as represented by the Treasurer's books and accounts, and said that this duty had been fulfilled. The report continued to say that the members of the committee had talked with the Treasurer *pro tempore* and had been assured by him that the examination had been thoroughly made and that to this extent the accountant's examination had been "verified" by the committee. The report added that if this represents the total obligations of the Auditing Committee, its work has been done. If, on the other hand, it is the duty of the Auditing Committee to afford assurance to the Council that the finances of the Society are adequately protected, the committee has not fulfilled its obligations, although it has been given assurance that auditing committees in the past have confined their efforts to what the present committee has done.

There were four specific recommendations contained in the report: first, that the investment of the Society's funds should be under the direction of a professional investment company; second, that the report of the accountant should be more com-

plete and include a list of investment transactions; third, that the latter should include a statement that the report of the fiscal year is reconciled with the report of the preceding year, and fourth, that the duties of the Auditing Committee be turned over to a business man trained as a bank examiner.

It was moved by Dr. Hamilton that the report be accepted. This motion was seconded by a councilor and it was so ordered by a vote of the Council.

It was moved by Dr. Francis P. Denny, Norfolk, that the recommendations contained in the report be referred to the Executive Committee. The motion was seconded by a councilor and it was so ordered by vote of the Council.

The Treasurer's report (Appendix No. 4) was offered by Dr. Eliot Hubbard, Jr., treasurer *pro tempore*. This report contained the following interesting information: the revenue of the Society from resident dues in 1942 was \$49,182.39 as compared with \$49,779.00 in 1941 and \$1738.25 from nonresident dues as compared with \$1670.75 in 1941. The total revenue from dues in 1942 was \$50,920.64.

Other revenue to the Society was \$3932.12 from invested funds (not including the Building Fund); \$17.30 from sales; \$288.65 from profits from the sales of securities; \$3287.75 from the sales of booths at the Annual Meeting; \$139.80 from subscriptions to the *Journal* from fellows in the service and \$558.00 from censors' examinations. This represents a total revenue of \$59,144.26, an increase of \$1444.96 over 1941. The income from the Building Fund was \$1844.19 plus \$72.66, the latter representing a profit from the sale of securities. The total Building Fund now stands at \$63,991.80. In 1942 the Society's total expenses were \$48,680.84. The unexpended revenue for the same year was \$10,463.42. This compares with a total expense in 1941 of \$45,310.47 and unexpended revenue that year of \$12,388.83. The Society ended the year of 1942 with total assets, cash and securities, of \$229,951.27 plus unexpended revenue of \$10,463.42.

There was much discussion at this point concerning the proper form in which reports offered to the Council should be handled by the Council. Should such reports be received, accepted or adopted? The President requested Dr. Frank R. Ober, Suffolk, to engage in research to this end. This the latter did. He read from *Robert's Rules of Order* to the effect that, although these terms are often used indiscriminately, the term "adopt" is preferable and least likely to be misunderstood.

Dr. Lester M. Felton, Worcester, moved that the Treasurer's report be accepted. This motion was seconded by a councilor and it was so ordered by vote of the Council.

REPORT OF EXECUTIVE COMMITTEE

This report (Appendix No. 5) was presented by the Secretary. The report spoke of two meetings which the committee held, one on October 21, 1942, and the other on December 30, 1942. The meeting held in October was of an emergency character and was called for the purpose of giving consideration to a vote adopted by the Massachusetts Board of Registration in Medicine, to wit:

Voted to ask the Governor of Massachusetts to waive the law (Chapter 112, Section 2, T. E.) to the effect that we may temporarily permit members of the medical profession, who are graduates of approved schools, who are registered to practice in other states and who are recommended by the National Procurement and Assignment Service, to practice in Massachusetts during the emergency without payment of the registration fee, and without examination.

The purpose of this action on the part of the Board was to facilitate the work of the Procurement and Assignment Service in relocating physicians during the present emergency and it was undertaken as a result of a conference between the Board, Dr. Lahey, Dr. Fitz and certain officers of the Massachusetts Medical Society. The report continued to say that Governor Saltonstall was willing to use his wartime emergency powers in this direction provided the Massachusetts Medical Society approved and that the Executive Committee, in the name of the Massachusetts Medical Society, gave its unanimous approval.

The Secretary moved that the Council approve this act of the Executive Committee. This motion was seconded by a councilor and it was so ordered by a vote of the Council.

The report spoke of the subsequent fate of this matter. The Attorney General, when approached for the purpose of actually drawing up the act, advised against it, because he was not convinced of its need in Massachusetts at that time. He made it clear, however, that he was without prejudice against the time when this need might arise in this state. He also spoke of the possibility of legislative action along this line. The report added that the committee had given consideration to this latter course of action, since such action had been urged by the Executive Committee of the Federation of State Medical Boards and recommends adversely on this particular proposition, because a directive from the Governor, when and if such a need develops, is much the simpler approach.

The Secretary moved the adoption of the recommendation. This motion was seconded by a councilor and it was so ordered by a vote of the Council.

The Executive Committee, acting on the recommendations of the Committee on Membership,

retired eleven fellows, restored eight to membership and accepted the resignations of four.

The committee approved of the recommendations contained in the reports of the Committees on Membership, Finance, Public Relations and Arrangements.

The committee commended to the Council the report of the Committee on Medical Education anent the nursing situation.

The committee recommended that the question of establishing a junior membership in the Massachusetts Medical Society, raised in a letter from Dr. Reginald Fitz, be referred to the Committee on Membership.

The Secretary moved the adoption of this recommendation. This motion was seconded by a councilor.

Dr. I. R. Jankelson, Norfolk, asked for a definition of junior membership. The Secretary suggested that Dr. Fitz might more properly answer this question. In reply, Dr. Fitz said that the matter will come up later in a report that he would submit. Dr. Jankelson thought that no action should be taken on this matter until more was known about it. The recommendation was adopted by vote of the Council.

The committee recommended the creation of a war-participation committee of five to be appointed by the President to act in conjunction with a similar committee of the American Medical Association. The Secretary moved the adoption of the recommendation. This motion was seconded by a councilor. Dr. Ernest L. Hunt, Worcester, asked what the duties of such a committee would be. The Secretary suggested to the President that Dr. Roger I. Lee, Suffolk, president-elect of the Massachusetts Medical Society and chairman of the Board of Trustees of the American Medical Association be permitted to answer Dr. Hunt's question.

Dr. Lee said that a war participation committee would take the place of the old Committee on War Preparedness, the functions of which latter committee have largely been taken over by a governmental agency, the Procurement and Assignment Service, which is responsible to the government and not in any way to medical societies. Dr. Lee added that it seemed desirable to have committees appointed by medical societies and responsible to them which could act as a sort of clearing house and liaison between the medical societies and Procurement and Assignment Service in the work that this latter agency is called on to do.

Dr. Hunt asked how such a committee could do anything without an appropriation. Dr. Lee replied that such a committee might need a modest appropriation. There was much discussion on the

matter, participated in by Dr. Robert N. Nye, Suffolk, Dr. Fitz and Dr. Carl Bearse, Norfolk.

The recommendation was adopted by vote of the Council.

The committee recommended that the request of Dr. Charles S. Butler, treasurer, for an indefinite leave of absence because of illness be granted, and that the Council express its very great thanks for his fine service to the Society and its regret that he had found such a step necessary. The Secretary moved the adoption of this recommendation. This motion was seconded by a councilor and it was so ordered by vote of the Council. The committee approved of the recommendation of the Committee on Finance that Dr. Butler's salary be paid to him up to and including December 31, 1942.

The Secretary acknowledged the receipt by the President of a letter dated January 28, 1943, in which Dr. Butler resigned as treasurer of the Massachusetts Medical Society. On a motion by the Secretary and a second by a councilor, this communication was laid on the table.

The committee acknowledged the receipt by the President of the following letter from Dr. William J. Brickley, Suffolk:

December 30, 1942

Dr. George Leonard Schadt, President
Massachusetts Medical Society
Boston, Massachusetts

Re: Gift to Massachusetts Medical Society

Dear Doctor:

Enclosed please find my check for \$1000 as a gift to the Massachusetts Medical Society, to be used in carrying out its usual functions as an educational body.

I would suggest that—though I do not make it a binding condition of the gift—this fund be used to procure any necessary lunches for the official meetings of the Committee on Ethics and Discipline. I have in mind the many hours spent and the difficult problems dealt with, not hastily, at such meetings.

Please advise me whether the Society will accept this gift.

Sincerely,

WILLIAM J. BRICKLEY, M.D.

The committee offered three recommendations with regard to this gift: that it be accepted by the Council with thanks; that it be used to create a fund which shall be known as the Dr. William J. Brickley Fund; and that it be used for the purpose outlined in Dr. Brickley's letter until otherwise ordered by the Council.

The Secretary moved the adoption of these recommendations. This motion was seconded by a councilor and it was so ordered by vote of the Council.

The committee had reviewed a list of appointments made by the President and had given them its approval.

The Secretary moved the adoption of the report of the Executive Committee as a whole. This motion was seconded by a councilor and it was so ordered by vote of the Council.

REPORTS OF COMMITTEES

Committee on Arrangements—Dr. Gordon M. Morrison, Middlesex South, chairman

The report, which was offered by Dr. Roy J. Heffernan, Norfolk, reads as follows:

I beg to submit herewith the report of the Committee on Arrangements. Owing to the present unsettled conditions surrounding us, the committee has three recommendations to make, all of which have been reviewed and approved by the Executive Committee: that the Council rescind its action of May, 1942, naming Springfield as the place of the annual meeting in 1943; that Boston be the place of the meeting in 1943; and that following the passage of the present emergency, the Council give serious consideration to Springfield as a suitable place for an annual meeting.

Dr. Heffernan moved the adoption of these recommendations. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Dr. Heffernan then made the following announcement:

Owing to the fact that the committee could not secure the proper hotel accommodations in Boston for May 17, 18 and 19, the Committee on Arrangements has changed the dates of the annual meeting. These new dates are May 24, 25 and 26.

The report as a whole was adopted by vote of the Council following a motion by Dr. Heffernan and a second by a councilor.

At this point it was explained to Dr. William A. R. Chapin, Hampden, that Dr. Spaid had sought retirement.

Committee on Publications—Dr. Richard M. Smith, Suffolk, chairman

This report (Appendix No. 6) said that Dr. George W. Thorn, Hersey Professor of the Theory and Practice of Physic at Harvard University and physician-in-chief at the Peter Bent Brigham Hospital, would deliver the Shattuck Lecture at the annual meeting.

It quoted Dr. Nye's report to the committee:

During 1942, the *New England Journal of Medicine* received 1984 new "outside" subscriptions, a total that is over 50 per cent greater than the total received in 1941. Of these subscriptions, 1085 were from regular subscribers and 899 from medical students. As would be expected, there were many cancellations, undoubtedly owing to enlistment in the armed forces; the net increases were 216 regular subscribers and 711 medical students, which total 927. As of December 31, 1942, journals were being sent to 5083 members of the

Society (a decrease of 74 from the 1941 figure), 3462 regular subscribers and 1193 medical students, a total of 9738, which is greater by 853 than the total for 1941. This does not include 348 members of the New Hampshire Medical Society, who receive the *Journal* once a month.

The editorial board took action on 238 manuscripts during 1942, a decrease of 90 compared with the figure for 1941. Of these papers, 169, or 71 per cent, were accepted.

There was a net loss of \$17,550 in operating the *Journal* in 1942. This represents \$3.43 per member of the Society and is approximately \$2450 less than the amount appropriated by the Society. The net cost per member was \$3.20 in 1941. A larger circulation, increased costs in binding and mailing, and fifty-three issues in 1942, a situation which arises every seven years, represent the reason for increased operating expenses in 1942.

It was stated that the operating expenses would probably be lower in 1943. This was predicated on a smaller total circulation and higher advertising rates, the latter being effective January 1, 1943. If it became a choice between cutting the pagination of the *Journal* or the acceptance of papers for publication below the *Journal's* present standards, the pagination would suffer the cut.

Dr. Smith moved the adoption of the report. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Membership—Dr. Harlan F. Newton, Suffolk, chairman

This report (Appendix No. 7) recommended adversely on the petition of Dr. Morris A. Cohen, 452 Beacon Street, Boston, for reinstatement to membership in the Massachusetts Medical Society.

Dr. Newton moved the adoption of this recommendation. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Dr. Walter Fenno Dearborn, 79 Fresh Pond Parkway, Cambridge, because of eminent work in the allied sciences, was recommended for associate fellowship in the Massachusetts Medical Society.

Dr. Newton moved the adoption of this recommendation. This motion was seconded by a councilor and it was so ordered by vote of the Council.

The committee offered the following recommendations:

1. That the following recommendation from the then Committee on Membership, passed by the Council February 5, 1941, be revoked: "Fellows of the Society who are called to full-time service in the United States Army, Navy or Public Health Service during the present emergency and whose livelihood is thereby impaired may, on written application to the Treasurer stating their situation, have their dues remitted for the year of service. A period of full-time service greater than six months shall give the privilege of a year's

remission of dues. The *New England Journal of Medicine* will be sent to such members only on payment of an annual fee of four dollars (\$4.00). The president of the Society shall determine the end of the present emergency."

2. That the following recommendation be passed: "Fellows of the Massachusetts Medical Society who have enlisted or been called to full-time service in the United States armed forces or in the United States Public Health Service during this present war shall have no further dues collected for the duration, their names continued on the membership roll of the Society as active members in good standing, and to only such members as request it will the *New England Journal of Medicine* be sent and then only on payment of an annual subscription fee of \$4.00 per year. Any members who have joined or who subsequently join the United States armed forces or the United States Public Health Service should advise personally or by some other means the Treasurer of the Society to facilitate omission of dues. 'For the duration' is interpreted as meaning honorable discharge from the United States armed forces or United States Public Health Service."

3. That a flyer of this recommendation be attached to every bill or communication relating to indebtedness sent from the Treasurer's office of the Massachusetts Medical Society to its members.

Dr. Newton moved the adoption of recommendation No. 1. This motion was seconded by a councilor.

Dr. James P. O'Hare, Suffolk, asked if this recommendation included withdrawal from the Council or from committees. He added that some men have the idea that they should drop their positions as councilors and others that they should not, and that this same holds true with regard to membership on some of the committees of the Suffolk District Medical Society. Dr. Newton replied that he thought it would apply to any councilor in any capacity. In reply to further questioning by Dr. O'Hare, Dr. Newton said that it was his view that the councilors referred to would lose their positions automatically. Dr. Schadt expressed a like view. Dr. O'Hare added that at least one such councilor had asked that he be retained in the Council.

Dr. Chapin asked what provision is made for the men who will continue in the service after the present emergency is over. He added that they might be carried for the rest of their lives, absolved of paying dues. Dr. Newton replied that he thought that was a matter which could be taken up at the end of the year.

Dr. John Homans, Suffolk, asked if the adoption of this recommendation will cause the Treasurer to refuse tender of dues on the part of those in the armed forces. Dr. Schadt at this point said that it was evident that much more thought and study should be given to this matter and suggested that it might be wise to refer the whole matter to the Executive Committee.

Dr. G. Colket Caner, Suffolk, said that he had worded the previous rules, after conversations with Dr. Butler. He said that it was their joint viewpoint that members who had entered the armed forces and who wished to continue to pay their dues should be permitted to do so. He said he approved of the leaflets which it was suggested should be added to the bills sent out by the Treasurer. He thought, however, that the old way of having the individual fellow decide for himself whether he should or should not request that his dues be remitted had many advantages. Dr. Newton replied that it was not the intent of the Committee on Membership to say to these fellows that they cannot pay their dues if they so desire.

Dr. Nye asked if the recommendation read that the Treasurer "shall not accept." Dr. Newton answered, "No." Dr. Nye asked for a reading of the first of recommendation No. 2. Dr. Newton read as follows:

Fellows of the Massachusetts Medical Society who have enlisted or been called to full-time service in the United States armed forces or in the United States Public Health Service during this present war shall have no further dues collected for the duration.

Dr. Nye asked if that did not mean that the Treasurer shall not accept dues even though they are sent in. Dr. Newton replied that it might be interpreted that way.

Dr. Walter G. Phippen, Essex South, asked if the former method was working any hardship on anybody. Dr. Newton replied in substance that this was partly so.

Dr. Donald Munro, Suffolk, suggested that the Council rescind the action of the Council as of February 5, 1941—recommendation No. 1—and refer the other recommendations to the Executive Committee. Dr. Nye pointed out that if this course were followed, the Society would have no means of remitting dues until such time as the Executive Committee had had time to act.

Dr. Caner thought that the whole matter might be covered quite well if a flyer were attached to each bill sent out by the Treasurer, calling each fellow's attention to the fact that, if they had entered the armed forces, they might have their dues remitted if they so desired and that these same men might continue to receive the *Journal* by the payment of \$4.00.

Dr. Elmer S. Bagnall, Essex North, thought this matter should be referred to the Executive Committee as a means of saving the Council's time.

Dr. Newton, with permission of the Council, withdrew his original motion as did the seconder. He then moved that the matter be recommended, for investigation and action, to the Executive Com-

mittee. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Finance—Dr. John Homans, Suffolk, chairman

The report was published in the *New England Journal of Medicine*, issue of January 14, 1943.

Dr. Homans, in offering this report, spoke of the difficulty in these times of actually forecasting the income of the Society. His committee thought that \$50.00 was a fair allowance for the expenses of a committee that was statewide in its composition.

He called attention to the expense of the Secretary's office which was more or less itemized. He said that the Secretary's office assumed many expenses of other committees and it was difficult to know where to assign these expenses. This was, however, he added, merely a matter of bookkeeping. He said that the same was true, to some extent, of the Treasurer's office. He pointed out that, now the bills for dues go directly to the members from this office, an item for the expense involved is included in the budget for that purpose. He said it might be necessary to employ a bookkeeper and that \$1000 was set down to cover this contingency.

He spoke of the rather large item in the budget to cover the maintenance of the Society's headquarters. He said that this was a rather complicated item and had to do with dealings between the Society, the *Journal* and the Boston Medical Library. He said that the *Journal* hires the various bookkeepers, clerks and so forth, and that the Society pays the *Journal* for their services to the extent that it uses them. Rent is paid not directly to the Boston Medical Library but through the *Journal*. Dr. Homans said that his committee has suggested to Dr. Robey that he and the Treasurer get together and produce something that all can understand. He spoke of the \$500 which was put down as a probable expense of holding the annual meeting and that it now was quite likely that this money would not be needed. He spoke of the reduction by \$5000 in the amount set down against the needs of the *Journal*.

Dr. Carl Bearse called attention to the by-law which requires that any expenditure of \$100 or more shall be broken down when so requested by a fellow. With this as a preamble, he requested that two large items, one for \$42,000, representing the publication cost of the *Journal*, and the other \$22,000 representing office and other salaries be broken down.

Dr. Homans broke down the second item as follows:

Editor	\$7,000
Associate editor	360
Associate editor	360
Assistant editor	3,000
Editor's assistant	1,380
Office secretaries	1,872
	1,664
	1,300
	1,040
	1,144
	936
	1,040
Total	\$21,096

With regard to the first item he read the following figures:

Printing	\$17,000
Stock	10,000
Binding and mailing	12,000
Engraving	3,000
Total	\$42,000

Dr. J. Harper Blaisdell, Middlesex East, made the following motion: First, under paragraph "Expenses of Officers and Delegates," that the item "Society Headquarters (general expenses) \$4500" be stricken out and, second, that under the paragraph "Standing Committees," that the sum of \$4500 be substituted for the zero after "Society Headquarters." Dr. Homans said he had no objection to this change. Dr. Fitz seconded the motion and it was so ordered by vote of the Council.

Dr. Channing Frothingham, Suffolk, moved that the report of the Committee on Finance be accepted. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Dr. Homans moved the adoption of the budget subject to the change indicated by Dr. Blaisdell's motion. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Ethics and Discipline—Dr. Ralph R. Stratton, Middlesex East, chairman

Dr. Stratton reported as follows:

Mr. President, the Committee on Ethics and Discipline has no stated report to make today. Either owing to the improved ethical morale of the members or to the fact that we have lost some of our troublesome problems, we have had very few complaints this last year.

On a motion by Dr. Stratton and a second by a councilor, this report was accepted by vote of the Council.

Committee on Medical Education—Dr. Robert T. Monroe, Norfolk, chairman

The complete report of this committee appeared in the *New England Journal of Medicine*, issue of January 14, 1943.

Dr. Monroe spoke as follows:

Our studies on the nursing situation created by the war have been printed in the January 14, 1943, issue of the *New England Journal of Medicine*. Our conclusions from these studies are that there is a shortage of nurses in this state and in the country, and that it is real, present and serious. This shortage of nurses does not appear to have come about as a result of shortsightedness on the part of responsible individuals. On the contrary, we have been impressed with the efforts of federal authorities and of hospital, civilian-defense and nursing executives to avert the shortage early and late. As we see it, the chief difficulty has been to get the workers—nurses for war work, pupils for graduate-nurse and attendant-nurse schools and women for ward helpers and Red Cross volunteer nurse's aides.

We believe that the needs of the armed forces can and will be met. The civilian-defense situation is fairly well in hand, for it is well organized and has a growing reserve of paid and volunteer workers; but there is no evidence that the reserve is large enough to meet an epidemic situation in the next few months. We are in doubt concerning the ability of hospitals to continue adequate nursing service for their patients for the duration of the war in times, such as the present, which are not obviously emergencies and therefore do not provoke the maximum efforts of all concerned. Hospitals are experimenting with various solutions and are getting the loyal co-operation of nurses and volunteers, but their position is far from secure.

Federal authorities have these matters under consideration and are in the process of deciding upon one or more solutions. We have heard of the plans and must confess that none seem ideal. However, one supplementary step might be taken at once, and that is to establish training schools in the large Army and Navy Hospitals. Teaching staffs could be assembled from the Army and Navy Nurses Corps and from civilian schools. Such schools could train easily several thousand pupils who in six months' time could become useful to those hospitals. Meanwhile it would appear to be the duty of every physician to foster in every possible way the growth and effectiveness of the graduate-nurse and attendant-nurse schools and the Red Cross volunteer-aide classes.

On a motion by Dr. Monroe and a second by a councilor the report was adopted by vote of the Council.

Committee on Public Health—Dr. Francis P. Denny, Norfolk, chairman

No report.

Committee on Medical Defense—Dr. Arthur W. Allen, Suffolk, chairman

No report.

Committee on Society Headquarters—Dr. William H. Robey, Suffolk, chairman

No report (see report of Committee to Aid the Boston Medical Library).

Committee on Industrial Health—Dr. Dwight O'Hara, Middlesex South, chairman

Dr. O'Hara spoke as follows:

On November 7 the Committee on Industrial Health held a morning, afternoon and evening program at the Harvard Club of Boston. Three hundred and eighteen persons, exclusive of speakers and committee members, registered, and when questioned responded to the effect that the meeting was not only worth while but worth repeating with another program. The committee is therefore arranging for a similar meeting, also to be held on a Saturday and at the Harvard Club, probably in April. The details of this meeting will be announced in the *New England Journal of Medicine*.

The committee has now had on file for some months the names and pertinent data concerning three hundred or more Massachusetts physicians who have signified their interest in and their availability for industrial medical practice. These data are also compiled on a punch-card system at the office of the Division of Occupational Hygiene of the State Department of Labor and Industries, and its availability was brought to the attention of the Associated Industries of Massachusetts at their annual meeting last fall. The fact that there have been only three or four inquiries from industrial plants seeking medical service, after what would seem to have been adequate publicity concerning this list, indicates that in Massachusetts at least the supply of industrial medical service is ample, and still is in excess of its demand.

Dr. O'Hara moved the adoption of the report. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Massachusetts Committee on Procurement and Assignment—Dr. Reginald Fitz, chairman

The report (Appendix No. 8), by courtesy of the committee, was presented by Dr. Fitz, who moved its adoption. This motion was seconded by a councilor and it was so ordered by vote of the Council.

The Council adjourned for luncheon at 1:00 p.m. and reassembled at 1:50 p.m.

Committee on Public Relations—Dr. Elmer S. Bagnall, Essex North, secretary

Dr. Bagnall reported as follows:

The committee held one meeting, on December 16, 1942, with members of the subcommittee on workmen's compensation hospitalized cases (Drs. Ellison, Gordon, Morrison and Scannell). The report of this subcommittee was considered and adopted and is recommended to you for adoption.

After conference with the Industrial Accident Board's advisory committee there was agreement with the Ellison subcommittee on the following:

(1) Freedom of choice in hospitalized cases should hereafter be defined as the selection by the injured (or his agent) of a physician from two lists, one containing the names of all physicians eligible to practice in the hospital concerned and the other the names of physicians submitted to the hospital by the insurer.

(2) The Ellison subcommittee was authorized to offer its support to the committee now revising the Industrial Accident Board's fee schedule.

The President invited the committee's attention to recent editorials and letters in the *Boston Herald* relating to our alleged attitude toward refugee physicians. The committee believes that organized medicine is misrepresented often enough to make it desirable that a subcommittee, not limited to the personnel of the Committee on Public Relations, be appointed to look into this matter and report to the Committee on Public Relations. If the committee finds ground for action you will then be asked whether you want a professional publicity agent to interpret fairly the attitude of the Society as the occasion arises.

Dr. Bagnall moved that the report be accepted and the recommendations adopted. The motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Tax-Supported Medical Care — Dr. Bagnall, chairman

This report was as follows:

The committee, through the chairman, is working in liaison with the Department of Public Welfare at the State House. There have been no matters of policy change necessitating a meeting of the entire committee. It seems desirable to continue the life of this committee despite the lull in current activities, so this is submitted as a report of progress.

Dr. Bagnall moved that the report be adopted as a report of progress. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Postpayment Medical Care (Bank Plan) — Dr. Bagnall, chairman

This report was as follows:

We are still awaiting the call of the committee from the Massachusetts Bankers Association who now hold the initiative.

Dr. Bagnall moved the adoption of this report. The motion was seconded and it was so ordered by vote of the Council.

Committee to Meet With the Medical Advisory Committee of the Industrial Accident Board — Dr. Daniel J. Ellison, Middlesex North, chairman

No response.

Committee on Prepayment Medical-Care Costs Insurance — Dr. James C. McCann, chairman

This report (Appendix No. 10) was presented by Dr. McCann, who moved its adoption. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Legislation — Dr. Brainard F. Conley, Middlesex South, chairman

Dr. Conley reported as follows:

This committee is now composed of eighteen members, one from each district of the Society, elected by ballot at the annual meeting of each district. The personnel of the committee at its start was as follows: Berkshire, P. J. Sullivan; Franklin, H. G. Stetson; Hampshire, J. D. Collins; Hampden, W. A. R. Chapin; Worcester North, H. D. Bone; Worcester, L. M. Felton; Essex North, E. H. Ganley; Essex South, C. A. Worthen; Middlesex North, W. H. Sherman; Middlesex East, K. L. MacLachlan; Middlesex South, B. F. Conley; Suffolk, W. B. Breed; Norfolk, D. L. Lionberger; Norfolk South, J. E. Knowlton; Plymouth, C. D. McCann; Bristol North, J. L. Murphy; Bristol South, E. H. Cody; Barnstable, not elected. There have been two resignations. D. L. Lionberger, of Norfolk, was the first to enlist in the service of his country and he has been succeeded by J. V. Fisher of their district. Shortly afterward, K. L. MacLachlan, of Middlesex East, enlisted and he has been succeeded by J. M. Wilcox. Both these men have done noble service for this society and they are now doing noble work for their country. This committee is proud of both of them. On October 21, 1942, on a call from the President, this committee met and organized. Brainard F. Conley, of Middlesex South, was elected chairman and Lester M. Felton, of Worcester, was elected secretary. It was voted that a committee of five members be appointed by the chairman, to consist of the chairman and four others, to act as a working committee, with authority to act for the full committee and that they be empowered to use their discretion in an emergency. The chairman has appointed the following four members: L. M. Felton, W. B. Breed, J. V. Fisher and C. D. McCann. This committee of five has already started going over the legislative petitions.

Because of so many members of the Society already in the armed forces of our country and more to go, we realize that the income of the Society will for this year be considerably lessened. For this reason we voted to discontinue the "Legislative Bulletin" for the duration.

The committee wishes to extend its thanks to the editor of the *New England Journal of Medicine* for his immediate willingness to publish, as often as necessary, such legislative matters as will be of interest to the members of the Society. We believe that this will have certain advantages over the bulletin, in that you will have knowledge of pending legislation much more promptly than heretofore. We therefore suggest that you watch each issue of the *Journal* from now on until the end of the present legislative year for your legislative information. After all, the *Journal* is the official organ of the Society.

Up to January 27, there have been twenty-eight petitions in the House of Representatives and four in the Senate which, in the opinion of the Legislative Reporting Service, are of concern to medicine. All these seem to be of more or less interest and are in the process of study as to their importance. So far there does not seem to be any incidence of new legislation. Some of the year-after-year bills are missing, at least up to now. For example, there is no "annual registration" petition, and the osteopaths and chiropractors are apparently occupied with things other than legislation.

We have published in the current issue of the *Journal* the whole of a petition which calls for the repeal of the provisions of the law requiring premarital serologic tests. This bill is marked for a hearing on March 11. We are inclined to believe we should lend our aid in retaining the blood test part of the present law.

There is another blood test bill which has come to our attention. It is numbered House 869 and reads as follows:

Every qualified physician shall, not less often than once in every period of six months submit to and take a blood test for the social diseases syphilis and gonorrhea, under rules and regulations promulgated therefor by the board of registration in medicine and shall at all times have permanently displayed in each of his offices or places of business a certificate of the board stating the date and the results of each last blood test.

We hope to have completed the study of all bills within the next two weeks and as soon as possible our recommendations as to action on each will be published, as well as the dates of hearings.

We have no recommendations to make at the present time.

Dr Conley moved the adoption of this report. The motion was seconded by a councilor and it was so ordered by vote of the Council.

Dr Conley called attention to the *Journal of the American Medical Association*, issue of January 23 1943, page 267, and advised all to read this material which represents the opinion of the court in affirming the guilt of the American Medical Association.

Committee on Cancer—Dr Shields Warren, Suffolk, chairman

No report

Committee on Postgraduate Instruction—Dr Reginald Fitz, Suffolk, chairman

No report

Military Postgraduate Committee—Dr W Richard Ohler, Jamaica Plain, chairman

No report

Committee on Physical Therapy—Dr Franklin P Lowry, Middlesex South, chairman

No report

Committee on Expert Testimony—Dr Frank R Ober, Suffolk, chairman

No report

Committee on Automobile Insurance Claims—Dr Henry C Marble, Newton Centre, chairman

No report

Committee on Convalescent Care—Dr T Duckett Jones, Roxbury, chairman

No response

Committee to Study the Practice of Medicine by Unregistered Persons—Dr Richard Dutton, Middlesex East, chairman

No report

Committee to Meet with Massachusetts Hospital Association—Dr Walter G Phippen, Essex South, chairman

No report

Committee to Examine WPA Records—Dr Guy L Richardson, Essex North, chairman

No report

Committee on Maternal Welfare—Dr Judson A Smith, Newton Centre, chairman

No report

Committee on Rehabilitation—Dr William E Browne, Suffolk, chairman

Dr Browne reported as follows:

There has been no occasion for this committee to meet since the last meeting of the Council and no meeting has been held. A few days ago a communication was received from the Subdivision on Health of the Massachusetts Committee on Public Safety. That communication states that a program is to be worked out whereby the Industrial Rehabilitation Division of the State Department of Education, through local rehabilitation agents now appointed, will determine which of those classified IV F in the draft may be returned to various war industries.

The plan anticipates that lay persons who have had some training as a nurse or social worker will review the confidential records indicating the cause for rejection of certain draftees. No action by the Council seems necessary on this matter at present. An expression of opinion would be appreciated from the Council concerning the desirability, if possible, of registered physicians in the Commonwealth reviewing these confidential matters with the hope of being of assistance to rehabilitation agents and others interested in returning a considerable number of men to various war industries. And so I have to report that that has just come to our attention.

Dr Browne moved the adoption of the report, this was seconded by a councilor and it was so ordered by a vote of the Council. He then moved that the Council recommend that these persons, rejected by selective service, should have their cases reviewed by a physician rather than by a lay person before they go into industry. This recommendation was seconded by a councilor. Dr Homans asked if this called simply for an expression of opinion by the Council. Dr Browne replied in the affirmative. It was so ordered by vote of the Council.

Committee to Aid the Boston Medical Library—
 Dr. William H. Robey, Suffolk, chairman

In the absence of Dr. Robey, the report was read by the Secretary, as follows:

It is the unanimous opinion of the Committee on Society Headquarters of the Massachusetts Medical Society that it is inadvisable to consider at the present time the purchase of a headquarters house for the Massachusetts Medical Society. Fellows in and out of Boston not members of the Committee have been asked about the desirability of having a house for the Society and not one has been found who has favored such an idea.

During the last six or seven years the Massachusetts Medical Society's use of the facilities offered by the Boston Medical Library has greatly increased, thereby causing added expense to the Boston Medical Library. The Library is used by members of the Society and almost constantly by the editorial staff of the *New England Journal of Medicine*, since all the communications to the *Journal* and especially the references to medical literature are confirmed in the Library.

The Boston Medical Library is the fourth largest medical library in the United States and therefore the thought that it must come to an end because of lack of funds cannot be tolerated. Various ways have been considered for increasing its membership but none have been successful largely because of the lack of interest of practitioners who live at a considerable distance from Boston. Even the membership of fellows living in Greater Boston is much smaller than it should be. The Committee on Finance proposes using the income of the Headquarters Building Fund for the Library. That income has varied in recent years from \$1800 to \$2200 per year. The money would probably be used to make the Library staff more efficient. There is a great need for training in library methods an assistant director who, if he proved to be of the right caliber, might in time be advanced to the position of director. An energetic young man in such a position would undoubtedly find the means of making the Library of far greater service to the members of the Massachusetts Medical Society than is the case at the present time. Those librarians who have been consulted in this matter are agreed that the value of many medical libraries has been greatly enhanced through the efforts of a director trained in modern library methods.

The Massachusetts Medical Society, the *New England Journal of Medicine* and the Boston Medical Library are inseparable. Medical schools and hospitals in many instances have their own working libraries, but the Boston Medical Library is and will continue to be the greatest reference library in this section of the country. We have the expectation of acquiring before long some additional space in the Library building which can be used for meetings of committees and other groups.

The Secretary pointed out that this report contained a recommendation that the income from the Headquarters Building Fund, amounting to between \$1800 and \$2200 per year, be turned over to the Boston Medical Library as a means of keeping

this valuable institution going. The Secretary moved the adoption of this recommendation and said that Dr. David Cheever, who likewise was unable to be present, wanted to be recorded in its favor. The motion was not seconded.

Dr. Charles E. Mongan, Middlesex South, objected to the adoption of this recommendation on the grounds that it calls for action that more properly should come under new business. He added that it came to us all as news that this situation had arisen. He moved that the whole matter be referred to the Executive Committee, that the attention and study which it deserves be taken by it and that its report be given at least twenty days before the annual meeting if it is possible to do so. This motion was not seconded.

Dr. Homans said he rather agreed with Dr. Mongan's idea. He added that from the point of view of the Committee on Finance, this matter of using some of the income of so-called funds for a permanent home has rather appealed to him. The income from funds of this kind that have been accumulating for a great while had better be used if some good use of the income can be found. If the dollar is devaluated 65 per cent the fund would not be what it was. So far as the Library is concerned, Dr. Homans added that he was one of its several directors and that the idea of this institution has always been to serve the Massachusetts Medical Society. Dr. Homans quoted Mr. Metcalf as saying that some attempt should be made to sell the Library to the medical public. Dr. Homans added that this has been successfully done in Chicago. The Boston Medical Library needs an active young man to put this over. The Library itself, without being in actual financial straits, is utterly incapable of doing this alone.

Dr. Fitz moved the acceptance of the report. This motion was seconded by Dr. Albert A. Horner, Suffolk, and it was so ordered by vote of the Council.

Dr. Conley asked the source of this \$1800 to \$2200 that it is proposed to turn over to the Boston Medical Library. Dr. Homans replied that it comes from the income of the Building Fund.

Dr. Hunt thought it would be enlightening to know how serious were the financial straits of the Library. Dr. Homans said that the Library was not in financial straits. It could continue to operate. It needed rehabilitation, however, and it did not have the funds to do it.

At this point Dr. Allen G. Rice, Hampden, asked Dr. Mongan to repeat his motion. Dr. Mongan again offered his original motion. It was seconded by Dr. Rice and it was so ordered by vote of the Council.

Committee on Ways and Means to Conserve Physicians' Energies—Dr Elmer S Bagnall, Essex North, chairman

This report (Appendix No 10) said that perhaps one third of the able bodied active practitioners of medicine are now withdrawn from their communities by the war effort. It added, however, that this will not seriously endanger the distribution of essential medical care except in certain areas where mushroomed growth of population has taken place.

It referred to Worcester as one center that had undertaken to utilize the services of hospitals in attempting to locate physicians in matters of emergency.

In Haverhill, physicians have volunteered to respond to night calls when the family physician is not available. For this service physicians are listed for each night and the telephone company is co-operating. The report spoke of the co-operation of a prominent pharmaceutical house in this work. It emphasized the fact that the method of handling this problem will vary with the community and that the medical profession of each community should take this responsibility to itself.

Hospitals should have the co-operation of their staff doctors to the end that hospital beds shall be used only by those who actually need them.

The report emphasized that these problems are very much in the minds of organized medicine and that, so far as Massachusetts is concerned, the Committee on Public Relations, because of the nature of its composition, would seem to be the clearing house for the initiation of remedies.

Dr Fitz commented on the importance of this report. He asked Dr Bagnall if he had any ideas concerning how the views that he put forward could be brought before the public and before the profession most forcibly.

Dr Bagnall replied that he thought that the matter should have a little more study and that the Committee on Public Relations might be able to devise the means of spreading the doctrine. Dr Bagnall continued as follows:

All of you probably saw the editorial in the *Herald* recently, I think about a week ago. It was very good. And there have been editorials in a lot of papers, and magazine articles. *Time* had an article, the *New York Times* had a special article in the Sunday magazine section. The idea is being broadcast, and I think in Massachusetts the whole state needs to consider it rather more than it has as yet. I think we in organized medicine rather tend to let these things go by default. If we are going to be considered by the Government we must do what we can to organize our house and fulfill our obligations in the distribution of medical care, so that they are more likely to consult us than if we default and they have to take over. I don't know that I have any specific recommendations beyond these.

Dr Bagnall moved that this report be accepted as a report of progress and that the committee co-operate with any other agency that may be made available to carry out these suggestions. This motion was seconded by Dr Mongrén and it was so ordered by vote of the Council.

APPOINTMENTS

Dr Schadt read a list of nominations.

Delegates and alternates to the House of Delegates American Medical Association from June 1, 1943 to June 1, 1945

Delegates	Alternates
Allen G Rice, Springfield	Patrick J Sullivan, Dalton
Richard H Müller, Boston	John Tallon, Worcester

Delegates to the annual meetings of the medical societies of the other New England States (except New Hampshire)

<i>Maine</i>	Warren H Sherman, Lowell, and Frank W Snow, Newburyport
<i>Vermont</i>	George D Henderson, Holyoke, and George L Steele, Springfield
<i>Rhode Island</i>	George A Buckley, Brockton, and Howard P Sawyer, Fall River
<i>Connecticut</i>	Ira M Dixon, Stockbridge, and Clarence E Burt, New Bedford

Delegate to the Annual Congress of the American Medical Association on Medical Education and Licensure at the Palmer House, Chicago February 15 and 16, 1943

Reginald Fitz Boston

Ad interim appointments to fill vacancies

COUNCIL

Dr Byron H Porter, Berkshire, replacing Dr I S I Dodd, who has become a member <i>ex officio</i>
Dr Frederick S Hopkins, Hampden, replacing Dr Oliver J Menard, resigned
Dr Benjamin S Wood, Middlesex South, replacing Dr Raymond A McCarthy, resigned
Dr David L Belding, Norfolk South, replacing Dr Robert L Cook, who has become a member <i>ex officio</i>
Dr Frederick W O'Brien, Suffolk, replacing Dr George C Shattuck, resigned
Dr Arthur W Marsh, Worcester, replacing Dr George C Tully, resigned
Dr Alfred P Lachance, Worcester North, replacing Dr Jesse C Hiles, resigned

BOARDS OF CENSORS

Dr George A Buckley, supervising censor, Plymouth, replacing Dr William T Hinson, resigned
Dr John A Putney, member of Board of Censors, Plymouth

COMMITTEE ON ARRANGEMENTS

Dr George G Bailey, replacing Dr Robert H Barker, resigned
--

COMMITTEE ON LICENSATION

Dr Charles D McCann, Plymouth, replacing Dr William T Hinson, resigned
--

COMMITTEE ON WAYS AND MEANS TO CONSERVE PHYSICIANS' ENERGIES

Dr. Elmer S. Bagnall, *chairman*
 Dr. Charles F. Wilinsky
 Dr. John J. Dumphry

Dr. Schadt asked if there were any nominations from the floor. Dr. J. Harper Blaisdell, Middlesex East, moved that they be confirmed. This motion was seconded by a councilor and it was so ordered by vote of the Council.

NEW BUSINESS

The President read the obituary of Dr. Charles Malone, a councilor from Norfolk District.

Dr. Charles Malone, councilor from the Norfolk District, died at his home in Jamaica Plain on October 10, 1942. He was in his sixty-eighth year.

Dr. Malone received his degree from Tufts College Medical School in 1902 and since that time had practiced in Jamaica Plain. He was a fellow of the American Medical Association.

Two sons and a daughter survive him.

At the request of the President, the Council stood in silence for one minute in tribute to the memory of Dr. Malone.

The Secretary presented a letter and enclosure (Appendix No. 11) which he had received from Dr. Henry M. Landesman, Norfolk.

Dr. Mongan moved that these matters be referred to the Committee on Legislation. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Dr. Hyman Morrison, Norfolk, urged greater support for the Boston Medical Library. He urged the councilors to get new members for the Library and suggested that hospital libraries might become participating members.

Dr. John Fallon, Worcester, made the following motion:

That the Executive Committee and the editors of the *New England Journal of Medicine* be instructed to investigate the feasibility of sending the *Journal* to each military station, having a medical library, at the expense of the Massachusetts Medical Society, that the Executive Committee be empowered to act in this matter and that the sum of \$400 be appropriated to that committee for that purpose.

Dr. Richard M. Smith, Suffolk, asked how many copies that would mean. He expressed the view that it might run into a considerable number of *Journals* and that the cost might be great.

Dr. Conley expressed the view that the men at Guadalcanal and Solomon Islands are not going to have much time to read the *Journal*.

Dr. Nye thought 800 copies might be needed and observed that \$400 would not go far under these circumstances.

Dr. Fallon remarked at this point that, in view of what had been said, it would be better if he withdrew the second part of his motion and left that part which empowered the Executive Committee only to look into the matter.

Dr. Homans suggested that the *Journal* ask members to donate journals. He expressed the viewpoint that if this was done many contributions would come in for this purpose.

Dr. Bearse suggested that a notice be printed in the *Journal*, directed to subscribers, asking them to return their journals, after they had read them, for transshipment to the Army libraries.

Dr. Nye expressed the view that probably as many as 75 journals are now going to Army hospitals.

Dr. Fallon's original motion, which was not seconded, was withdrawn by him. He offered the following motion:

That the Executive Committee and the editors of the *New England Journal of Medicine* be instructed to investigate the feasibility of sending the *Journal* to each military station, having a medical library, at the expense of the Massachusetts Medical Society.

This motion was seconded by Dr. Fitz and it was so ordered by vote of the Council.

Dr. Harold R. Kurth, Essex North, made the following statement to the Council:

I wish to draw your attention to a matter which presented itself to the local membership committee of the Essex North District Medical Society. This matter arose in the course of the examination of one of its applicants for membership in the Massachusetts Medical Society just previous to the last censors' meeting. Having presented the facts in this case, I should like to call on the members of the Council for a sense-of-the-meeting vote.

An applicant, who is a graduate of the University of Kansas City Medical School in 1932, licensed to practice medicine in Massachusetts in 1937, applied, on July 17, 1942, for admission to the Massachusetts Medical Society. His application was sponsored by a reputable member of the profession in his community, and forwarded to the district secretary, together with six letters of recommendation from colleagues of high professional standing in this district. The Essex North local membership committee met, examined and interrogated the applicant very closely and, as a result of that examination and close interrogation, was of the unanimous opinion that he should be recommended for fellowship in the Society. I might state here and now that the local membership committee of Essex North takes its work very seriously and investigates all applicants, particularly those of unapproved or foreign schools. Unless they meet its unqualified approval the committee does not hesitate to refuse their applications for membership in the Society. This has been amply demonstrated in the past by the number of applicants who have been refused fellowship in the Society.

The chairman of the central committee on membership was duly notified by the secretary that "it is the

unanimous opinion of this committee, after due investigation, and close interrogation that the applicant be recommended for fellowship in the Society. The local membership committee was somewhat surprised when it received word that the central committee on membership did not approve the application in spite of the fact that it had been unanimously endorsed by the local committee. The reasons given by the chairman of the central committee were that his educational qualifications were rather dubious. The local committee maintains that it already fully realized that situation, but felt, nevertheless, that it was in a better position to pass judgment on the man's qualifications for membership than was a group of men who in all probability did not know him at all. Furthermore, the local committee felt that his educational qualifications would be no different in two years than they were at the present time!

The second reason given by the central committee was that the local committee was not particularly enthusiastic and that his recommending letters were not particularly informative. The local committee in answer to this criticism, states that it feels that it is not necessary for the local committee to eulogize its applicants, and that when the local committee unanimously approves an applicant for fellowship in the Society, it means exactly that, and nothing else. The recommending letters of the applicant were honest expressions of opinions of physicians of high standing in his district, and due emphasis should be placed on these letters of recommendation.

The third criticism as stated by the chairman of the central committee was that it was of the greatest importance that the district membership committee should show that the district society wants that applicant as a member. To this criticism the local committee replies that the Massachusetts Medical Society is representative of the highest standard of medical practice and medical ethics, and is the organization with which all physicians aspire to become identified. Therefore the applicant seeks the Society and not the Society the applicant!

The purpose in presenting this matter to you is that it was felt by the Essex North local committee that it had spent a great deal of time in investigating his man's qualifications, it had spent almost an hour in interviewing this man and as a result had unanimously approved his application. Yet in spite of all this work, and in spite of the fact that this man was endorsed by a group of men for whom the local membership committee has the highest regard his application was rejected by the central committee for the reasons which have been discussed above. It is felt by the local committee that if the opinion of the local committees in general is to be upset by the central committee for such inadequate and unsubstantial reasons, that the function of the local committees will become purely superfluous in character. When Dr John Monks of the Suffolk District, introduced the change in the by laws with reference to application for fellowship in the Massachusetts Medical Society at the special meeting held on April 9, 1941, he stressed in speaking of the local committee, as follows:

The Committee on Medical Education and Medical Diplomas has sensed for a long time how helpful it was in obtaining adequate information on which to determine the desirability of candidates for

fellowship this point has already been discussed more fully in the formal report. It is believed that a local board will be in every way better fitted to obtain this information than the central committee. The number of men on the board is small, they are already in positions of responsibility in their local society, and two of the three are already members of the board of censors, which eventually will examine those candidates finally approved. Further, it is very definitely felt that in the case of graduates of unrecognized schools the essential responsibility of whether or not they should be admitted to membership in the local society should lie with their own nearby colleagues not with those farther afield.

He furthermore stated: The central committee shall take the responsibility of seeing that on the one hand undue pressure has not been brought to bear on the local board to recommend for approval an undesirable applicant nor on the other hand that unwarranted local prejudice bar from approval a desirable applicant. It does seem, then that the responsibility for recommending or turning down applicants for fellowship should rest with the local committee under the supervision of the central committee. I might state furthermore that this was the opinion in the minds of Dr J H Blaisdell's by laws committee in reviewing the mechanism for application for fellowship in the Society. It is the feeling of the local membership committee of Essex North that the principles, as expressed by Dr Monks and Dr Blaisdell's committees, have been disregarded in this case and that should this policy be continued, the important work of local committees will be jeopardized and must eventually become purely superfluous.

We have brought this matter to the attention of the Council because we are firmly convinced that the present by laws for application for membership to the Massachusetts Medical Society are adequate and desirable. An applicant is tried and approved by his colleagues who are in an excellent position to know the type of professional ethics which this applicant practices far better than a group of men who in all probability know nothing of the applicant at all! It is hoped that the principles expressed by Dr Monks will continue to dominate the endorsement of all new applicants to the Society.

Dr Kurth made the following motion:

It is the sense of this meeting that the essential responsibility of whether or not graduates of unrecognized or foreign schools shall be admitted to the Society lies in the local membership committees and that the central committee should concern itself essentially with the responsibility of seeing that no undue pressure has been brought to bear upon the local boards either to endorse or to bar, the approval of candidates.

Dr Bagnall in seconding the motion said the issue was clear. Either the local committee should do the job it ought to do or else the local committee should be discarded.

Dr Roy V Brackett, Essex North, spoke of how carefully the applicant had been examined and

how thoroughly the question of his acceptance had been discussed. He said that no change in the by-law is desired. The by-law is entirely adequate. Its administration, however, requires some attention.

Dr. Norman A. Welch, Norfolk, called the attention of the Council to the fact that, while the present by-laws were in the making, he tried to provide a means of appeal to the Executive Committee in cases of this sort. He added that he does not think this situation will arise often but, when and if it does, there is no means of handling it.

Dr. Fitz asked for a reading of the by-laws as they relate to this matter.

Dr. Schadt read from the by-laws as follows:

The Committee on Membership shall have custody of such documents so long as needed and then shall deliver them to the custody of the Secretary; they shall remain *confidential*.

The Committee on Membership shall consider the application of each applicant approved for censors' examination by a board of membership. It shall determine finally whether or not such applicant may take that examination.

The Committee on Membership shall not consider the application of any applicant disapproved by a board of membership except on the written request of a majority of that board of membership.

Dr. Mongan asked for a rereading of the motion. Dr. Kurth complied and added that he did not propose any change in the by-laws and that his motion was not in conflict with these laws. He simply wished to determine the meaning of this new mechanism that has been set up—in other words, whether the responsibility of determining if a man is eligible lies with the local committee or with the central committee.

In answer to Dr. Blaisdell, Dr. Kurth said that all he was trying to get by his motion was the sense of the meeting.

Dr. Fitz expressed the thought that there were not enough councilors present at this time for the Council to pass a sense-of-the-meeting vote. There was some discussion at this point about a quorum. This issue, however, was not formally raised.

Dr. Kurth withdrew his motion and Dr. Bagnall his second with the consent of the Council.

Dr. Mongan moved that further discussion on this matter be postponed to the next meeting and that this matter be made the first order of business. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Dr. Mongan moved that the Executive Committee consider some method of attendance that would cause councilors to remain until the business of the Council is completed. Dr. Fitz seconded the motion.

In supporting his motion Dr. Mongan referred to the meetings of the House of Delegates of the American Medical Association. He pointed out that each delegate was required to sign an attendance slip at every session and that the record of attendance was published, so that it might become generally known who were and who were not attending to their duties. He added that this had a salutary effect.

The motion was adopted by vote of the Council. The Council adjourned at 3:30 p.m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE

BARNSTABLE

C. H. Keene
W. D. Kinney

BERKSHIRE

J. J. Boland
I. S. F. Dodd
Solomon Schwager

BRISTOL NORTH

R. M. Chambers

BRISTOL SOUTH

C. C. Tripp

ESSEX NORTH

E. S. Bagnall
L. R. Chaput
J. P. Creed
H. R. Kurth
P. J. Look
R. C. Norris
G. L. Richardson
F. W. Snow

ESSEX SOUTH

Bernard Appel
H. A. Boyle
C. L. Curtis
Loring Grimes
B. B. Mansfield
O. S. Pettingill
W. G. Phippen
E. D. Reynolds
H. D. Stebbins
C. F. Twomey
C. A. Worthen

FRANKLIN

H. G. Stetson

HAMPDEN

W. C. Barnes
W. A. R. Chapin
A. J. Douglas

E. C. Dubois
Adolph Franz, Jr.
G. L. Gabler
P. E. Gear
Frederic Hagler
G. D. Henderson
A. G. Rice
G. L. Schadt
G. L. Steele

MIDDLESEX EAST

J. H. Blaisdell
Richard Dutton
E. M. Halligan
R. W. Layton
R. R. Stratton

MIDDLESEX NORTH

D. J. Ellison
W. H. Sherman
M. A. Tighe

MIDDLESEX SOUTH

C. F. Atwood
E. W. Barron
W. B. Bartlett
Harris Bass
J. M. Baty
G. F. H. Bowers
Madeline R. Brown
R. W. Buck
E. J. Butler
J. F. Casey
B. F. Conley
H. F. Day
C. L. Derick
H. Q. Gallupe
H. G. Giddings
H. W. Godfrey
Eliot Hubbard, Jr.
L. H. Jack
F. R. Jouett
A. A. Levi
A. N. Makechnic
Dudley Merrill
C. E. Mongan

J. P. Nelligan
S. J. G. Nowak
E. J. O'Brien, Jr.
Dwight O'Hara
L. G. Paul
E. H. Robbins
M. J. Schlesinger
E. F. Sewall
E. W. Small
H. W. Thayer
A. B. Toppam
J. E. Vance
B. M. Wein
B. S. Wood
Hovhannes Zovickian

NORFOLK

J. R. Barry
Carl Bearse
Arthur Berk
M. I. Berman
G. F. Blood
L. F. Curran
F. P. Denny
Albert Ehrenfried
H. M. Emmons
J. C. V. Fisher
Susannah Friedman
David Glunts
J. B. Hall
R. J. Heffernan
I. R. Jankelson
C. J. Kickham
E. L. Kickham
D. S. Luce
T. F. P. Lyons
R. T. Monroe
F. J. Moran
Hyman Morrison
M. W. O'Connell
H. C. Petterson
S. A. Robins
S. M. Saltz
D. D. Scannell
Kathleyne S. Snow
J. W. Spellman
J. P. Treanor, Jr.
N. A. Welch

NORFOLK SOUTH

D. L. Belding
D. B. Reardon
H. A. Robinson

PLYMOUTH

P. H. Leavitt
G. A. Moore

APPENDIX NO. 2

REPORT OF THE AUDITING COMMITTEE FOR YEAR ENDED
DECEMBER 31, 1941

The report of the examination of the books and accounts
of the Massachusetts Medical Society for the twelve

SUFFOLK

H. L. Albright
A. W. Allen
W. B. Breed
W. J. Brickley
W. E. Browne
G. C. Caner
E. M. Chapman
David Cheever
Pasquale Costanza
G. B. Fenwick
Reginald Fitz
Maurice Fremont Smith
Channing Frothingham
Joseph Garland
John Homans
A. A. Hornor
R. I. Lee
W. J. Mixer
Donald Munro
H. L. Musgrave
H. F. Newton
R. N. Nye
F. R. Ober
F. W. O'Brien
J. P. O'Hare
Helen S. Pittman
W. H. Robey
R. M. Smith
E. F. Timmins
S. N. Vose
Shields Warren
C. F. Wilnsky

WORCESTER

J. I. Ashkins
J. C. Austin
Gordon Berry
W. P. Bowers
G. A. Dix
J. M. Fallon
L. M. Felton
E. L. Hunt
W. F. Lynch
A. W. Marsh
J. C. McCann
A. E. O'Connell
R. S. Perkins
C. A. Sparrow
R. J. Ward
R. P. Watkins

WORCESTER NORTH

E. A. Adams
H. C. Arey
H. D. Bone
G. P. Keaveny
A. P. Lachance
B. P. Sweeney

months ended December 31, 1941, made by Messrs. Hartshorn and Walter, of Boston, has been submitted to the attention of the Auditing Committee.

As the Auditing Committee, we have carefully examined the report of these certified public accountants, and approve the figures submitted by them.

LEROY A. SCHALL, *Chairman*
JOHN ROCK

* * *

January 30, 1942.

The Auditing Committee:

Dr. LeRoy A. Schall
Dr. John Rock

The Massachusetts Medical Society

9 The Fenway
Boston, Massachusetts

Gentlemen:

At the request of your treasurer, Dr. Charles S. Butler, we have examined the books and accounts of the Massachusetts Medical Society for the twelve months ended December 31, 1941, and submit herewith:

SCHEDULE A: Statement showing the balance sheet of the Massachusetts Medical Society, December 31, 1941.

SCHEDULE B: Statement showing the revenue and expenses of the Massachusetts Medical Society for the twelve months ended December 31, 1941.

The cash balance on December 31, 1941, was verified by direct correspondence and reconciliation. The cash receipts as recorded have been deposited in the bank and disbursements are supported by vouchers or canceled checks.

The securities and savings-bank books were examined or accounted for.

The accompanying balance sheet and related statement of revenue and expenses fairly present the position of the Massachusetts Medical Society on December 31, 1941, and the results of operations for the year ended on that date.

Respectfully submitted,
HARTSHORN AND WALTER.

50 Congress Street
Boston

* * *

SCHEDULE A

STATEMENT SHOWING THE BALANCE SHEET OF THE MASSACHUSETTS MEDICAL SOCIETY, DECEMBER 31, 1941

ASSETS		
Fund Securities and Cash		
Endowment Funds	\$22,166 87	
Building Fund	62,074 95	
General Fund	132,595 40	
Total		\$216,837.22
LIABILITIES AND FUND ACCOUNTS		
Fund Accounts		
Endowment Funds		
Shattuck Fund		
G C Shattuck, 1854-1896	\$9,166 87	
Phillips Fund		
Jonathan Phillips, 1860	10,000 00	
Cotting Fund		
B L Cotting, \$1,000 — 1876 1891 1897	3,000 00	
		22,166 87
Building Fund		62,074 95
General Fund		132,595 40
Total		\$216,837.22

SCHEDULE A EXHIBIT 1

ENDOWMENT FUNDS, DECEMBER 31, 1941

	Securities and Cash	Income
Shattuck Fund		
Annuity Policy — Massachusetts Hospital Life Insurance Co. Certificate No. 438	\$9,166 87	\$183.34
Phillips Fund		
\$10,000 Commonwealth of Massachusetts 3½s Jan. 1, 1944 (Reg.)	10,000 00	350.00
Cotting Fund		
Deposit — Institution for Savings in Roxbury, No. 45252	1,000 00	20 00
Deposit — Provident Institution for Savings, Boston, No. 1828	1,000 00	20.00
Deposit — Suffolk Savings Bank, No. 68364	1,000 00	15.00
Totals	\$22,166 87	\$588.34

4,000 U. S. A. Defense Bonds Series F Dated May, 1941, Due 12 Yrs. from Date	2,960 00	
3,000 U. S. A. Treasury Bonds 2½s 1952-54 (Registered)	3,000 00	54.24
2,000 Virginian Ry. Co. 1st & Ref. Mtg. Series A 3½s, Mar. 1, 1966	2,045.00	75.00
1,000 Youngstown Sheet & Tube Co. 1st Mtg. Series D 3½s, Nov. 1, 1960	1,030.00	32 50
— Boston Medical Library Note, Extended to Apr. 1, 1942, @ 3%..	19,000 00	688 75
Totals	\$62,074.95	\$1,899 06
Less bond premiums charged off		16 67
Net income transferred to Building Fund Principal		\$1,889 06

SCHEDULE A EXHIBIT 3

GENERAL FUND, DECEMBER 31, 1941

SCHEDULE A EXHIBIT 2

BUILDING FUND DECEMBER 31, 1941

	Securities and Cash	Income	Premium Charged Off
Cash — New England Trust Co., Boston	\$2,678 19		
Deposit — Framingham National Bank Savings Dept., Book No. 8592	379 60	\$4 69	
Deposit — Franklin Savings Bank, Book No. 172838	1,884 04	37 11	
\$1,000 Bethlehem Steel Corp. 3½s Cons Mtg. Series H, Feb. 1, 1965	1,000 00	32 50	
1,000 Blackstone Valley Gas & Electric Series C 4s, Nov. 1, 1965	1,025 00	40 00	
1,000 Boston & Albany R.R. 1st Mtg. Series A 4½s, Apr. 1, 1943, Guaranteed	967 50	45 00	
1,000 Canada, Dominion of, 3s, Nov. 15, 1968	972 50	30 00	
— Central Illinois Public Service Co. 1st Mtg. Series A 3½s, Dec. 1, 1968		75 00	
1,000 Central Pacific Ry. Co. 1st Ref. Mtg. 4s, Aug., 1949	717 80	40 00	
1,000 Chicago, Burlington & Quincy R.R. Co. 4s, Mar. 1, 1958	977 78	40 00	
5,000 C/D Chicago, R. I. & Pacific Ry. 1st Ref. 4s, Apr. 1, 1934 (In Default), Written Down	400 00		
5,000 Conveyancers Title Insurance & Mortgage Co. Part Mtg. 4½s, Oct. 31, 1939 (In Default), Written Down	1,162 09	60 55	
1,000 City of Quincy, Mass., 3½s, May 1, 1943	1,016 00	35 00	
1,000 Connecticut River Power Co. 3½s Series A, Feb. 15, 1961	1,045 00	37 50	
1,000 Elgin, Joliet & Eastern Ry. Co. 1st Mtg. 3½s Series A, Mar. 1, 1970	1,015 00	32 50	
1,000 Kansas City, Mo., 4½s, Dec. 1, 1945	1,040 00	42 50	
1,000 Louisville & Nashville R.R. Co. 3½s 10 Yr. Unified, Extended to Jan. 1, 1950	1,010 00	52 50	
1,000 Louisville & Nashville R.R. Co. 4s 20 Yr. Gold Unified, Extended to Jan. 1, 1960	1,005 00	60 00	
1,000 Monongahela Ry. Co. 3½s Feb. 1, 1966, 1st Mtg. Series B	1,025 00	13 36	
2,000 N. Y. Central R.R. S. F. Sec. 3½s, Apr. 1, 1946	1,960 00	75 00	
1,200 N. Y., Chicago & St. Louis R.R. Notes 6s, June 1, 1950	1,200 00	72 00	
800 Pittsburgh & West Virginia Equipment Trust 3½s, Apr. 1, 1944	801 25	17 12	
1,000 Quebec, Province of, 3s, July 15, 1952	984 14	30 00	
2,000 Shell Union Oil 2½s Deb., July 1, 1954	1,930 56	15 98	
1,000 Southern Pacific Co. Equip. Trust Series R 2½s, June 1, 1944	1,035 60	9 00	
1,000 Southern Pacific Co. Equip. Trust Series R 2½s, June 1, 1945	1,037.90	9 00	
500 Swampscott, Mass., Series D 3½s, Sept. 1, 1942	510 00	17 50	\$10.00
1,000 The Texas Corp. C 3s, May 15, 1965	1,030 00	30 00	
2,000 Toledo Edison Co. 1st Mtg. 3½s, July 1, 1968	2,030.00	70 00	
— U. S. A. Treasury Note Series A 1½s, Mar. 15, 1941		7.50	
200 U. S. A. Treasury Bond 2½s, June 15, 1954-56	200 00	2.26	
1,000 U. S. A. Treasury 2½s, Sept. 15, 1950-52	1,000.00	25.00	
1,000 U. S. A. Treasury Bond 2s, Dec. 15, 1950 48	1,000.00	10.00	

	Securities and Cash	Income	Premium Charged Off
Cash — Merchants National Bank, Boston	\$9,865 51		
Cash — New England Trust Company, Boston	4,503 31		
Deposit — Franklin Savings Bank Book No. 35649	1,074.48	\$21 48	
— Appalachian Electric Power Co. 4s, Feb. 1, 1963		56 34	
\$2,000 Atlantic Coast Line R.R. Co. 1st Cons. Mtg. 4s, July 1, 1952	1,503 04	80.00	
2,000 Bethlehem Steel Corp. 3½s Cons. Mtg. Series H, Feb. 1, 1965	2,000 00	65 00	
3,000 Blackstone Valley Gas & Electric Co. Series D 3½s, Dec. 1, 1968	3,142.50	105 00	
1,000 Blackstone Valley Gas & Electric Co. Series C 4s, Nov. 1, 1965	1,025 00	40 00	
2,000 Boston & Albany R.R. 1st Mtg. 4½s, Apr. 1, 1943 (Guaranteed)	1,935.00	90 00	
— Boston Elevated Ry. 4½s, Nov. 1, 1941		127.50	\$87 50
1,000 Canadian National Railways Equip. Trust Series L 4½s, June 1, 1945	1,015.00	29 25	
1,000 Canadian Pacific Ry. Equip. Trust Series C 4½s, Dec. 1, 1943	1,070 00	45 00	16 25
2,000 Carolina, Clinchfield & Ohio Ry. Series A 4s, Sept. 1, 1965	2,050 00	80 00	
— Central Illinois Public Service Co. 1st Mtg. Series A 3½s, Dec. 1, 1968		75 00	
— Chesapeake & Ohio R.R. (Warm Springs Valley Branch) Gold 5s, Sept. 1, 1941		25 00	10 00
5,000 Chesapeake & Ohio Ry. Co. Ref. & Imp. 0.85% Series G, Feb. 1, 1944	5,000 00	17.47	
2,000 Chicago, Burlington & Quincy R.R. Co. 1st Ref. Series A 5s, Feb. 1, 1971	2,155.70	100 00	
5,000 City of Cleveland Water Works 5s, June 1, 1942	5,110.00	6 94	5 50
2,000 City of Providence, R. I., Sewer Loan 4½s, Apr. 1, 1942	2,052.50	90 00	60 00
— Commonwealth of Mass. 3½s, Jan. 1, 1941 (Reg.)		17.50	
1,000 Commonwealth of Mass. 3½s, Jan. 1, 1942 (Reg.)	1,020 00	35 00	20 00
1,000 Connecticut River Power Co. 1st 3½s Series A, Feb. 15, 1961	1,045.00	37 50	
2,000 Consolidated Edison Co. of N. Y. Inc. 3½s Deb., Jan. 1, 1958	2,035.00	70 00	
2,000 Consumers Power Co. 1st Mtg. 3½s, Nov. 1, 1969	2,110 00	65 00	
2,000 Conveyancers Title Insurance & Mortgage Co. 4½s, Dec. 1, 1937 (In Default), Written Down	400 00		
5,000 Eastern Railway Co. of Minnesota 1st Mtg. 4s, Apr. 1, 1948 (Reg.)	5,270.00	200 00	30 00
— Elgin, Joliet & Eastern Ry. Co. Series A 1st Mtg. 3½s, Mar. 1, 1970		104 00	
2,000 Erie Railroad Co. Ohio Div. 3½s, Sept. 1, 1971 (Temporary Certificate)	2,000.00	10 83*	
1,000 Fort Street Union Depot Co. 1st Mtg. 3½s, Dec. 1, 1965	1,000.00	37.50	
— General Motors Acceptance Corp., Dec. 31, 1941		21 88	
2,000 Great Northern Ry. Co. Gen. Mtg. B 5½s, Jan. 1, 1952	1,932.50	110 00	
1,000 Great Northern Ry. Co. 1st & Ref. 4½s, July 1, 1961	990.30	42.50	
1,000 Great Northern Ry. Co. Gen. Mtg. Gold Series I 3½s, Jan. 1, 1967	975.00	37.50	
2,000 Hiram Walker-Gooderham & Worts Ltd., 50%, Nov. 1, 1942	2,000.00	.67*	

2 000 Hiram Walker-Gooderham & Worts Ltd, 1 00% Nov 1 1943	2 000 00	1 33*
1 000 Jacksonville Terminal Co Series B 6s Ref & Ext Mtg Gold July 1 1967	1 065 00	60 00
1 000 Jersey Central Power & Light Co 3 1/2s 1st Mtg Mar 1 1955	1 025 00	59*9
1 000 Louisville & Nashville R R Co 3 1/2s Unified Mtg Extended to Jan 1 1950	1 010 00	1*50
1 000 Louisville & Nashville R R Co 4s Unified Gold Extended to Jan 1 1960	1 005 00	20 00
3 000 International Paper Co Ref Series A 6s Mar 1 1955	3 076 00	180 00
— Jones & Laughlin Steel Co 1st Mtg Series A 4 1/2s Mar 1 1961		21 25
— Koppers Co 1st & Col Trust Series A 4s Nov 1 1951		21 00
— Lone Star Gas Corp 3 1/2s S T Deb Aug 1 1953		20 42
2 000 Metropolitan Ice Co 1st Mtg Series A 7s Jan 1 1954	2 100 00	140 00
1 000 Monongahela Ry Co 1st Mtg Series B 3 1/2s Feb 1 1966	1 075 00	13 36
540 National Bondholders Corp Partic Crt (In Default)	540 00	
2 000 New Brunswick Province of Deb 3s July 1 1944	2 000 00	60 00
1 000 New Brunswick Province of Deb 3 1/2s July 1 1949	1 000 00	35 00
2 000 New York Connecting R R Co 1st Mtg Series A 3 1/2s Oct 1 1965	2 040 00	0 00
— New York State of World War Bonus Fund 4 1/2s Apr 1 1941		85 00
1 000 N Y Central R R Co S F 3 1/2s Apr 1 1946 (Secured)	980 00	37*0
1 000 N Y Cl & So & St Louis R R Co 1st Mtg 3 1/2s Extended to Oct 1 1947	93 50	35 00
600 N Y Chicago & St Lou s R R 6% Notes June 1 1950	600 00	36 00
1 000 Ohio Edison Co 1st Mtg 4s Sept 1 1967	1 005 00	8*8
— Peoples Gas Light & Coke Co 1st & Ref Series D 4s June 1 1961		30 11
1 000 Quebec Province of 3s July 15 1950	995 17	30 00
3 000 Remington Rind Inc S F Deb 3 1/2s July 1 1956 (Temporary Crt)	3 117 50	8 5*
1 000 Revere Copper & Brass Inc 1st Mtg 3 1/2s Nov 15 1960	1 075 00	3*0
2 000 Richmond Terminal Ry Co 1st Mtg 3 1/2s Sept 1 1965	2 100 00	7*50
2 000 So Pacific (Ore Lines) 1st Mtg Series A 4 s Mar 1 19	1 605 00	90 00
1 000 So Pacific Co Equip Trust Series R 2 1/2s June 1 1944	1 035 60	9 00
1 000 So Pacific Co Equip Trust Series R 2 1/2s June 1 1945	1 037 92	9 00
2 000 Texas Corp Deb 3s Apr 1 1959	2 020 00	00 00
2 000 Texas Corp 3s May 15 1965	2 060 00	00 00
1 000 The Dow Chemical Co Del 2 1/2s Sept 1 1950	1 015 00	22 50
1 000 Toledo Edison Co 1st Mtg 3 1/2s July 1 1968	1 015 00	35 00
5 000 Town of Springfield Vt 2 1/2s Nov 15 1942	5 045 00	*50 45 00
— Troy N Y (Harbor & Docks) 4 1/2s July 1 1941		85 00
3 000 Union Pacific Equip Trust Series G 1 1/2s Oct 1 1943 (Temporary Crt)	3 057 48	3 25*
3 000 U S Defense Bonds Series G Dated May 1941 Due 12 Yrs from date	3 000 00	3*50
2 200 U S A Treasury 3 1/2s Oct 15 1945 43	2 709 00	1*50
— U S A Treasury 3 1/2s Aug 1 1941		65 00
3 000 U S A Treasury 3 1/2s Oct 15 1945 43	3 041 25	97 50
— U S A Treasury 1 1/2s Series A Mar 15 1941		7 50
3 000 U S A Treasury 1 1/2s Series A Mar 15 1942	3 003 44	57 50
2 000 U S A Treasury 2s 1955 51 (Registered)	2 000 00	
3 000 U S A Treasury 2 1/2s 1972 67 (Registered)	3 000 00	64
500 U S Treasury Note 3 1/2s Dec 15 1945	500 00	3 71
— U S Steel Corp 3 1/2s May 1 1941		5 00
1 000 The Virginian Ry Co 1st Len & Ref Mtg Series A 3 1/2s Mar 1 1966	1 022 50	37 50
1 000 Westinghouse Elec & Mfg Co Deb 2 1/2s Nov 1 1951 (Temporary Crt)	1 015 00	1 18*
3 000 Wilson & Co Inc Series A 1st Mtg 4s July 15 1955	3 000 00	170 00
New England Journal of Medicine	1 00	

Manchester Conn Note Aug 15 1941	4 00
Lawrence Mass, Note Nov 14 1941	5 63
Totals	\$132 595 40
Less bond premiums charged off	\$3 847 04
	354 25
Net Income	\$3 492 79

*Interest paid out

SCHEDULE A EXHIBIT 4

BUILDING FUND DECEMBER 31 1941

Balance January 1 1941	\$60 069 95
Additions	
Income from securities	\$1 899 06
Profit on securities sold	115 94
Total additions	2 015 00
Total	\$72 084 95
Deduct on	
Bond premiums charged off	10 00
Balance December 31 1941	\$62 074 95

SCHEDULE A EXHIBIT 5

GENERAL FUND DECEMBER 31 1941

Balance January 1 1941	\$122 188 47
Addition	
Unexpended revenue for the twelve months ended December 31 1941	17 388 83
Total	\$134 577 30
Deductions	
Library Extens on Service	\$1 681 90
Veneral Disease Control	300 00
Total deductions	1 981 90
Balance December 31 1941	\$132 595 40

SCHEDULE B

STATEMENT SHOWING THE REVENUE AND EXPENSES OF THE MASSACHUSETTS MEDICAL SOCIETY FOR THE TWELVE MONTHS ENDED DECEMBER 31 1941

REVENUE	
Assessments Received by District Treasurers	
Barnstable	\$230 00
Berkshire	1 220 00
Bristol North	675 00
Bristol South	1 990 00
Essex North	1 912 00
Essex South	2 960 00
Franklin	430 00
Hampden	3 220 00
Hampshire	380 00
Middlesex North	260 00
Middlesex South	9 630 00
Middlesex East	1 680 00
Norfolk	800 00
Norfolk South	1 740 00
Plymouth	1 385 00
Suffolk	6 410 00
Worcester	4 010 00
Worcester North	980 00
Assessments Received by Treasurer	\$4* 918 00
Nonresident Assessments	1 861 00
Sale of Directorates and History	1 670*5
Received from Committee of Arrangements	13 54
Received for Journal from Fellows on active service	1 065 05
Examination Fees Received by Censors	37 00
Income from Funds	
Endowment Funds	\$585 34
General Fund	3 492*9
Profit on Sale of Securities—General Fund	4 651 13
Total Revenue	\$57 799 30

EXPENSES

Salaries		
Secretary	\$737 50	
Secretary Pro Tem	750 00	
Executive Secretary	2,800 80	
Treasurer	1,800 00	
	<u>\$6,088 30</u>	
Expenses of Officers and Delegates		
President	\$174 08	
Secretary	2,407 35	
Treasurer	304 55	
District Treasurers	2,628 25	
Censors	603 00	
Delegates to American Medical Association	427.31	
	<u>6 544 54</u>	
General Expenses		
Maintenance of Society Headquarters (including clerical and other expenses)	\$4,463 90	
Shattuck Lecture	200 00	
Cotting Luncheons	485 00	
Standing Committees		
State and National Legislation	3,850 76	
Public Health	25 00	
Medical Education and Diplomas	19 37	
Ethics and Discipline	58 81	
Public Relations	415 60	
Financial Planning and Budget	22 75	
Obstetrics and Gynecology	110 00	
Publications		
A New England Journal of Medicine	\$17,400 00	
B Annual Directory	202 22	
C Miscellaneous expense	70	
	<u>17,602 92</u>	
Medical Defense	853 78	
Medical Preparedness	22 65	
Postgraduate Instruction	230 66	
Executive Committee Expenses	105 00	
	<u>28,466 20</u>	
Refunds to District Societies		4,000 00
Refunds to Fellows on active service for six months or more	198 00	
Miscellaneous Expenses	13 43	
	<u>45,310 47</u>	
Total Expenses		
Unexpended Revenue		<u>\$12,388 83</u>

APPENDIX NO. 3

REPORT OF AUDITING COMMITTEE FOR YEAR ENDED
DECEMBER 31, 1942

We have examined a statement made by Hartshorn and Walter, accountants and auditors, 50 Congress Street, Boston, submitted to us January 28. They state that they have verified the cash balance by direct correspondence and reconciliation; that the cash receipts as recorded have been deposited and that disbursements are supported by vouchers or canceled checks; and that the securities and related statement of revenue and expenses fairly present the position of the Society on December 31, 1942, and the results of operations for the year ended on that date. They have submitted a statement showing the balance sheet of the Society on December 31, 1942, and a statement showing the revenue and expenses for the Society for the twelve months ended December 31, 1942. There is nothing in the statements concerning the investments made or closed during 1942 or whether there is an increase or decrease in the capital investment.

The by-laws state that the duty of the Auditing Committee is to require examination by a certified public accountant of the assets and securities of the Society in the custody of the Treasurer and the Treasurer's books and accounts. We have talked with the Assistant Treasurer and he has assured us that Hartshorn and Walter have done this thoroughly.

It is also the duty of the Auditing Committee to verify the accountant's examination. In so far as above stated,

we have "verified" the accountant's examination. We have not examined the Treasurer's books and accounts nor have we checked the actual assets and securities of the Society.

If the duties of the Auditing Committee as interpreted by the Council are to review the report of the certified public accountant as submitted in order to save the Council's time, the committee believes that it has performed its function. If the duties of the Auditing Committee as interpreted by the Council are to afford assurance to the Council that the finances of the Society are adequately protected, we have not in our opinion fulfilled them. We have been assured that, in the past, auditing committees have confined their work to what we have done.

It is our unverified opinion based on conversations with officers in the Society and a study of the by-laws pertaining to finances and a study of the accountant's report for the year ended December 31, 1942, that the finances of the Society have been and are well administered but that this is due to the unusual ability and devotion of the officers concerned. We do not believe that the Society can feel that its funds are protected by the by-laws. We believe that investments should be under the direction of a professional investment company, and that the report of the accountant should be more complete and include a list of investment transactions. It should also include a statement that the report for the current year is reconciled with the report of the preceding year.

We believe that the duties of the Auditing Committee could better be discharged by a business man trained as a bank examiner.

FRANCIS COOLEY HALL, *Chairman*
BURTON E. HAMILTON

* * *

January 29, 1943

The Auditing Committee:

Francis C. Hall

Burton E. Hamilton

The Massachusetts Medical Society

8 The Fenway

Boston, Massachusetts

Gentlemen:

At the request of your treasurer, Dr. Charles S. Butler, we have examined the books and accounts of the Massachusetts Medical Society for the twelve months ended December 31, 1942, and submit herewith:

SCHEDULE A: Statement showing the balance sheet of the Massachusetts Medical Society, December 31, 1942.

SCHEDULE B: Statement showing the revenue and expenses of the Massachusetts Medical Society for the twelve months ended December 31, 1942.

The cash balance on December 31, 1942, was verified by direct correspondence and reconciliation. The cash receipts as recorded have been deposited in the bank and disbursements are supported by vouchers or canceled checks.

The securities and savings-bank books were examined or accounted for.

The accompanying balance sheet and related statement of revenue and expenses fairly present the position of the Massachusetts Medical Society on December 31, 1942, and the results of operations for the year ended on that date.

Respectfully submitted,
HARTSHORN AND WALTER.

SCHEDULE A

STATEMENT SHOWING THE BALANCE SHEET OF THE MASSACHUSETTS MEDICAL SOCIETY DECEMBER 31 1942

ASSETS

Fund Securities and Cash

Endowment Funds	\$22 166 87
Building Fund	63 991 80
General Fund	143 792 60

Total	\$229 951 27
-------	--------------

LIABILITIES AND FUND ACCOUNTS

Fund Accounts

Endowment Funds	
Shattuck Fund	
G. C. Shattuck 1834 1866	\$9 166 87
Phillips Fund	
Jonathan Phillips 1860	10 000 00
Cotting Fund	
B. E. Cotting \$1 000 — 1876 1881 1887	3 000 00
Building Fund	
General Fund	
Total	\$29 951 27

SCHEDULE A EXHIBIT I

ENDOWMENT FUNDS DECEMBER 31 1942

	Securities and Cash	Income
Shattuck Fund		
Annuity Policy — Massachusetts Hospital Life Insurance Co Certificate No 438	\$9 166 87	\$163 34
Phillips Fund		
\$10 000 Commonwealth of Massachusetts 3 1/2% Jan 1 1944 (Reg)	10 000 00	3 00 00
Cotting Fund		
Deposit — Institution for Savings in Roxbury No 45252	1 000 00	20 00
Deposit — Provident Institution for Savings Boston No 1878	1 000 00	70 00
Deposit — Suffolk Savings Bank No 63364	1 000 00	15 00
Totals	\$22 166 87	\$388 34

SCHEDULE A EXHIBIT 2

BUILDING FUND DECEMBER 31 1942

	Securities and Cash	Income	Premium Charged Off
Cash — New England Trust Co	\$3 917 15		
Deposit — Framingham National Bank Savings Dept Book No 8592	383 40	\$3 80	
Deposit — Franklin Savings Bank Book No 17238	1 921 50	37 86	
— Bethlehem Steel Corp Cons Mtg Series H 3 1/4% Feb 1 1965		19 77	
1 000 Blackstone Valley Gas & Electric Series C 4 1/2% Nov 1 1965	1 025 00	40 00	
— Boston & Albany R.R. 1st Mtg Series A 4 1/2% Apr 1 1943 (Guaranteed)		32 13	
1 000 Canadian Dominion of Sts Nov 15 1965	972 50	30 00	
1 000 Central Pacific Ry Co 1st Ref Mtg 4 1/2% Aug 1949	717 80	40 00	
1 000 Chicago Burlington & Quincy R.R. Co 4 1/2% Mar 1 1958	977 78	40 00	
5 000 C/D Chicago R.I. & Pacific Ry 1st Ref 4 1/2% Apr 1 1934 (In Default) Written Down	400 00		
4 963 73 Conveyancers Title Insurance & Mortgage Co Parts Mtg 4 1/2% Oct 31 1939 (In Default) Written Down	1 125 82	102 41	
1 000 Connecticut River Power Co Series A 3 1/2% Feb 15 1961	1 045 00	37 50	
1 000 Elgin Joliet & Eastern Ry Co 1st Mtg Series A 3 1/2% Mar 1 1910	1 015 00	32 50	
1 000 Kansas City Mo. 4 1/2% Dec 1 1945	1 030 00	42 50	\$10 00
1 000 Louisville & Nashville R.R. Co 3 1/2% 10 yr Unfied Extended to Jan 1 1950	1 010 00	35 00	
1 000 Louisville & Nashville R.R. Co 4 1/2% 20 yr Gold Unfied Extended to Jan 1 1960	1 005 00	40 00	

1 000 Monongahela Ry Co 1st Mtg Series B 3 1/2% Feb 1 1966	1 075 00	32 50	
2 000 N.Y. Central R.R. S.F. Sec 3 1/2% Apr 1 1946	1 960 00	75 00	
1 200 N.Y. Chicago & St. Louis R.R. Notes 6 1/2% June 1 1950	1 200 00	72 00	
800 Pittsburgh & West Virginia Equipment Trust 3 1/2% Apr 1 1944	801 25	28 00	
1 000 Pittsburgh City of C 4 1/2% Dec 1 1945	1 040 00	26 75	4.58
1 000 Quebec Prov. nec. of 3 1/2% July 15 1952	984 14	30 00	
1 000 Quincy Mass 3 1/2% May 1 1943	1 016 00	35 00	
2 000 Shell Un on O 1 Dec 2 1/2% July 1 1951	1 930 56	50 00	
1 000 Southern Pacific Co Equip. Trust Series R 2 1/2% June 1 1944	1 032 60	22 50	
1 000 Southern Pacific Co Equip. Trust Series R 2 1/2% June 1 1945	1 037 90	22 50	
— Swampscott Mass Series D 3 1/2% Sept 1 1942	17 50	10 00	
— Texaco Corp Series C 3 1/2% May 15 1955	15 92		
2 000 Toledo Edison Co 1st Mtg 3 1/2% July 1 1968	2 030 00	70 00	
200 U.S.A. Treasury Bond 2 1/2% June 15 1954 56	200 00	4 50	
1 000 U.S.A. Treasury 2 1/2% Sept 15 1950 52	1 000 00	25 00	
1 000 U.S.A. Treasury Bond 2 1/2% Dec 15 1950 48	1 000 00	20 00	
4 000 U.S.A. Defense Bonds Series F 2 1/2% Dated May 1941 Due 1 1/2 Yrs from Date	2 960 00		
3 000 U.S.A. Treasury Bonds 2 1/2% 1952 54 (Reg)	3 000 00	75 00	
2 000 Virginian Ry Co 1st & Ref Mtg Series A 3 1/2% Mar 1 1966	2 045 00	75 00	
1 000 Youngstown Sheet & Tube Co. 1st Mtg Series D 3 1/2% Nov 1 1960	1 030 00	32 50	
— Boston Medical Library Note Extended to Apr 1 1943 @ 3%	19 000 00	570 00	
30 Shs G. C. Murphy Co Pfd 4 1/2%	3 150 00	35 63	
Totals	\$63 991 80	\$1 878 77	\$54 58
Less bond premiums charged off		24 58	
Net income transferred to Building Fund principal		\$1 844 19	

SCHEDULE A EXHIBIT 3

GENERAL FUND DECEMBER 31 1942

	Securities and Cash	Income	Premium Charged Off
Cash — Merchants National Bank Boston	\$7 940 86		
Cash — New England Trust Company Boston	8 606 46		
Deposit — Franklin Savings Bank Book No 35649	1 074 48	\$21 48	
— Amer. Can. Tobacco Co 3 1/2% Apr 15 1962		80 59	
\$ 000 Athens Coast Line R.R. Co 1st Cons Mtg 4 1/2% July 1952	1 503 04	80 00	
— Bethlehem Steel Corp Cons Mtg Series H 3 1/2% Feb 1 1965		56 15	
3 000 Blackstone Valley Gas & Electric Co Series D 3 1/2% Dec 1 1968	3 142 50	105 00	
1 000 Blackstone Valley Gas & Electric Co Series C 4 1/2% Nov 1 1965	1 025 00	40 00	
— Boston & Albany R.R. 1st Mtg 4 1/2% Apr 1 1943 (Guaranteed)		57 00	
1 000 Canadian National R.R. 1st Mtg Equip. Trust Series L 4 1/2% June 1 1945	1 015 00	45 00	
1 000 Canadian Pacific R.R. 1st Mtg Equip. Trust Series C 4 1/2% Dec 1 1943	1 070 00	45 00	
2 000 Carolina Cl. nchfield & Ohio Ry. Sec. res A 4 1/2% Sept 1 1965	2 050 00	80 00	
5 000 Chesapeake & Ohio Ry. Co Ref. & Imp. Series G 0.85% 3 1/2% Feb 1 1944	5 000 00	42 50	
2 000 Chicago Burlington & Quincy R.R. Co 1st Ref Series A 5 1/2% Feb 1 1971	2 155 00	100 00	
— Cleveland City of Water Works 5 1/2% June 1 1942		175 00	\$110 00
1 000 Connecticut River Power Co 1st Series A 3 1/2% Feb 15 1961	1 045 00	37 50	
— Consolidated Edison Co. of N.Y. Inc. Deb 3 1/2% Jan 1 1958		52 50	
2 000 Consumers Power Co 1st Mtg 3 1/2% Nov 1 1960	2 110 00	65 00	
2 000 Conveyancers Title Insurance & Mtg Co 4 1/2% Dec 1 1937 (In Default) Written Down	400 00		
1 000 Duval Chem. Co. Dec 2 1/2% Sept 1 1950	1 015 00	27 50	

5 000 Eastern Railway Co of Minnesota 1st Mtg 4s, Apr 1, 1948 (Reg)	5,270 00	200 00	
2 000 Erie Railroad Co Ohio Div 3½s, Sept 1 1971	2,000 00	65 00	
1,000 Fort Street Union Depot Co 1st Mtg 3½s, Dec 1, 1965	1,000 00	37 50	
2 000 Great Northern Ry Co Gen Mtg B 5½s, Jan 1, 1952	1 932 50	110 00	
1 000 Great Northern Ry Co 1st & Ref 4½s July 1, 1961	990 30	42 50	
1 000 Great Northern Ry Co Gen Mtg Gold Series I 3½s, Jan 1, 1967	975 00	37 50	
— Hiram Walker-Gooderham & Worts Ltd ½s Nov 1, 1942		10 00	
2 000 Hiram Walker-Gooderham & Worts Ltd 1s Nov 1 1943	2 000 00	20 00	
1,000 Jacksonville Terminal Co Series B Ref & Ext Mtg Gold 6s July 1, 1967	1 065 00	60 00	
— Jersey Central Power & Light Co 1st Mtg 3½s Mar 1, 1965		27 90	
1,000 Louisville & Nashville RR Co 3½s Unified Mtg Extended to Jan 1, 1950	1 010 00	35 00	
1 000 Louisville & Nashville RR Co 4s Unified Gold Extended to Jan 1, 1960	1,005 00	40 00	
2 500 International Paper Co Ref Series A 6s Mar 1 1955	2 563 33	165 00	
— Massachusetts Commth of 3½s Jan 1 1942 (Reg)		17 50	20 00
2 000 Metropolitan Ice Co 1st Mtg Series A 7s Jan 1 1954	2 080 00	140 00	20 00
1 000 Monongahela Ry Co 1st Mtg Series B 3½s Feb 1 1966	1,025 00	32 50	
3 000 National Bondholders Corp Partic Ctf (In Default)	390 00		
2 000 New Brunswick Province of Deb 3s, July 1 1944	2 000 00	60 00	
1 000 New Brunswick Province of, Deb 3½s July 1, 1949	1 000 00	35 00	
— Newbury Mass Note Dec 15, 1942		33 75	
2 000 New York Connecting R R Co 1st Mtg Series A 3½s Oct 1, 1965	2 040 00	70 00	
1 000 New York Central R R S F 3½s, Apr 1 1946 (Secured)	980 00	37 50	
1 000 N Y Chicago & St Louis RR Co 1st Mtg 3½s Extended to Oct 1, 1947	937 50	35 00	
600 N Y Chicago & St Louis RR Co 6% Notes June 1, 1950	600 00	36 00	
1 000 Ohio Edison Co 1st Mtg 4s Sept 1 1967	1 005 00	40 00	
— Pittsfield Mass, Due Nov 23, 1942		9 64	
— Providence City of R 1, Sewer Loan 4½s Apr 1 1942		45 00	52 50
1 000 Quebec Province of 3s July 15, 1950	995 37	30 00	
3 000 Remington Rand Inc S F Deb 3½s July 1 1956	3 112 50	105 00	
1 000 Revere Copper & Brass Co 1st Mtg 3½s Nov 15, 1960	1 025 00	32 50	
2 000 Richmond Terminal Ry Co 1st Mtg 3½s Sept 1 1965	2 100 00	67 50	
2 000 So Pacific (Ore Lines) 1st Mtg Series A 4½s Mar 1 1977	1 605 00	90 00	
1 000 So Pacific Co Equip Trust Series R 2½s June 1 1944	1 025 00	22 50	10 60
1 000 So Pacific Co Equip Trust Series R 2½s June 1 1945	1 037 92	22 50	
— Springfield Vt 2½s, Nov 15 1942		112 50	45 00
2 000 Texas Corp Deb 3s Apr 1, 1959	2 020 00	60 00	
— Texas Corp 3s May 15 1965		4 91	
1 000 Toledo Edison Co 1st Mtg 3½s July 1 1968	1 015 00	35 00	
5 600 Troy N Y, 4½s Feb 1 1943	5,031 64	74 38*	
3 000 Union Pacific Equip. Trust Series G 1½s Oct 1 1943	3 040 00	45 00	17 48
3 000 U S Defense Bonds G 2½s dated May 1941, Due 12 yrs from date	3 000 00	75 00	
2 200 U S A Treasury 3½s, Oct 15 1945-43	2 200 00	71 50	
3 000 U S A Treasury 3½s Oct 15 1945 43	3 025 00	97 50	16 25
— U S A Treasury Series A 1½s Mar 15 1942		17 40	
2 000 U S A Treasury 2s 1955 51 (Reg)	2 000 00	40 00	
5 000 U S A Treasury 2s, 1949 51	5,000 00	33 42	
3 000 U S A Treasury 2½s, 1972 67 (Reg)	3,000 00	67 75	
500 U S Treasury Note ½s Dec 15, 1945	500 00	3 75	
2 000 U S A Treasury 7½s Nov 2, 1943	2,000 00		
1 000 Virginian Ry Co 1st Lien & Ref Mtg Series A 3½s, Mar 1, 1966	1,022 50	37 50	
1,000 Westinghouse Electric & Mfg Co Deb 2½s, Nov 1, 1951	1,015 00	21 25	
3 000 Wilson & Co Series A 1st Mtg 4s, July 15, 1955	3 000 00	120 00	

Massachusetts Medical Service—De mind Loan	25 000 00		
New England Journal of Medicine	1 00		
Totals	\$143,792 60	\$3 635 61	\$791 81
Less bond premiums charged off		291 83	
Net Income		\$3 343 78	

*Interest paid out

SCHEDULE A EXHIBIT 4

BUILDING FUND, DECEMBER 31, 1942

Balance January 1, 1942		\$67 074.50
Additions		
Income from Securities	\$1,668 77	
Profit on Securities Sold	72 66	
Total Additions		1 941 43
Total		\$64 016.33
Deduction		
Bond Premiums Charged Off		24 58
Balance, December 31, 1942		\$63 991 81

SCHEDULE A EXHIBIT 5

GENERAL FUND, DECEMBER 31, 1942

Balance January 1 1942		\$132 595 49
Additions		
Expenses included in 1942 but entered in Cash Book in January, 1943	\$1,650 03	
Unexpended Income for the Twelve Months ended December 31, 1942	10 463 42	
Total Additions		12 113 45
Total		\$144 708 95
Deductions		
Amount received from New England Journal of Medicine in January, 1943, credited on books in December, 1942	\$900 00	
November coupon of Revere Copper & Brass, Inc., included in 1942 income but not deposited	16 25	
Total Deductions		916 25
Balance December 31, 1942		\$143 792 60

SCHEDULE B

STATEMENT SHOWING THE REVENUE AND EXPENSES OF THE MASSACHUSETTS MEDICAL SOCIETY FOR THE TWELVE MONTHS ENDED DECEMBER 31, 1942

REVENUE		
Assessments Received by District Treasurers		\$48 666 39
Assessments Received by Treasurer		516 00
Nonresident Assessments		1 738 25
Sale of Directories and Royalties		17 30
Received from Committee of Arrangements		3 287 70
Received for Journal from Fellows on Active Service		139 63
Examination Fees Received by Censors		525 00
Income from Funds		
Endowment Funds	\$588 34	
General Fund	3 343 78	
Profit on Sale of Securities—General Fund		3 932 17
Total Revenue		\$29 144 76

EXPENSES

Salaries		
Secretary	\$3 000 00	
Executive Secretary	3,000 00	
Treasurer	1,500 00	
		\$7,500 00

Expenses of Officers and Delegates

President	\$191 52
Secretary	3 243 37
Treasurer	574 69
District Treasurers	2 469 19
Censors	273 00
Delegates to American Medical Association	408 24
	<u>7,112 01</u>

General Expenses

Maintenance of Society Headquarters (including clerical and other expenses)	\$4 256 82
Shattuck Lecture	200 00
Cotting Luncheons	447 50
Legislation	21 02
Public Health	10 70
Medical Education and Diplomas	873
Ethics and Discipline	47 96
Public Relations	1 934 47
Examination of W P A Records	2 74
Memberships	9 35
Finance	96
Publications	
<i>A New England Journal of Medicine</i>	\$19 100 00
<i>B Directors</i>	<u>1 841 53</u>
Revision of By Laws	297 34
Medical Defense	822 02
Postgraduate Instruction	694 55
Executive Committee Expenses	<u>130 96</u>
	<u>29 876 07</u>

Refunds to District Societies	4 000 00
Refunds to Fellows on Active Service	16 00
Listing Members in Forces	170
Miscellaneous Expenses	<u>174 51</u>
Total Expenses	<u>48 680 84</u>
Unexpended Revenue	<u>\$10 463 42</u>

Expenses of Officers and Delegates

President	174 08	193 52
Secretary	2407 35	3243 37
Treasurer	304 55	574 69
District treasurers	2628 25	2469 19
Censors	603 00	273 00
Delegates to American Medical Association	<u>427 31</u>	<u>408 24</u>

General Expenses

Maintenance of Society Headquarters	4463 90	4256 82
Shattuck Lecturer	200 00	200 00
Cotting Luncheons	<u>485 00</u>	<u>447 50</u>

Committee Expenses

Publications		
<i>A New England Journal of Medicine</i>	17 400 00	19 100 00
<i>B Annual Directory</i>	202 92	1841 53
Ethics and Discipline	58 81	47 96
Medical Education and Diplomas	19 37	8 73
State and National Legislation	3850 76	21 02
Public Health	25 00	10 70
Medical Defense	853 78	822 02
Public Relations	415 60	1934 42
Postgraduate Medical Instruction	230 66	694 55
Medical Preparedness	22 65	—
Financial Planning and Budget	22 75	96
Executive Committee	105 00	130 96
Examination of WPA Records	—	2 74
Memberships	—	9 35
Revision of By Laws	—	<u>297 34</u>

Special Appropriations

Statistics and Cynecology	110 00	—
Refund to district societies	4000 00	4000 00
Refunds to fellows on active service	158 00	16 00
Miscellaneous	13 43	<u>174 51</u>
Listing members in forces	—	<u>170</u>

Total expenses	<u>\$45 310 47</u>	<u>\$48 680 84</u>
Unexpended revenue	<u>12 388 83</u>	<u>10 463 42</u>
	<u>\$57 699 30</u>	<u>\$59 144 26</u>

APPENDIX NO 4

REPORT OF THE TREASURER

It is unfortunate that Dr Butler cannot be with us to present the Treasurer's report for 1942, but his illness has made this impossible. It has also prevented his compiling a report.

Therefore I am simply submitting the bare figures for 1942 without any personal comments.

In 1942, revenues from resident dues were \$49,182 39 as compared with \$49,779 00 from the same source in 1941. Nonresident dues were \$1738 25 as compared with \$1670 75 in 1941. The combined annual dues were there for \$50,920 64. Other revenues were as follows from invested funds (not including the Building Fund), \$3932 12, from sales, \$17 30, from profits on securities sold, \$288 65, from booths at the annual meeting, \$3287 75, received for the *New England Journal of Medicine* from fellows in active service, \$139 80, and from examinations by censors, \$558 00. Hence the total revenue to the Society amounted to \$59,144 26, an increase of \$1444 96 over 1941.

The Building Fund received an income of \$1844 19 and profit from sales of securities amounted to \$72 66. The total Building Fund now stands at \$63,991 80.

In 1942, total expenses were \$48,680 84, with an unexpended revenue of \$10,463 42 as compared with total expenses of \$45,310 47 and an unexpended revenue of \$12,388 83 in 1941.

The Society ends 1942 with total assets of cash and securities of \$229,951 27, and unexpended revenues of \$10,463 42.

ELIOT HUBBARD, JR., Treasurer pro tempore

REVENUE OF FINANCES FOR 1942 IN COMPARISON WITH 1941

	1941	1942
Salaries		
Secretary and Secretary pro temp	\$1487 50	\$3000 00
Executive Assistant	2800 80	3000 00
Treasurer	1800 00	1500 00

REVENUES

	1941	1942
Assessments		
<i>P</i> By resident fellows		
To district treasurers	\$47 918 00	\$48 676 39
To Treasurer	1861 00	516 00
Paid by nonresident fellows	1670 75	1738 25
Sales of Directory and History	13 54	17 30
Income		
Shattuck Fund	183 34	183 34
Phillips Fund	350 00	350 00
Cotting Fund	55 00	55 00
General Fund	3492 79	3343 78
Other Revenue		
From Committee of Arrangements	1065 05	\$387 75
Received from fellows for <i>Journal</i>	32 60	139 80
Received for examinations by censors	243 00	558 00
Profits on sales of securities	814 83	288 65
	<u>\$57 699 30</u>	<u>\$59 144 26</u>

APPENDIX NO 5

REPORT OF THE EXECUTIVE COMMITTEE

The Executive Committee of the Council has had two meetings since its report to the Council in October. The first of these was held on October 21, 1942, and the second on December 30, 1942.

The October meeting was of an emergency character. It was called for the purpose of giving consideration to a proposition advanced by the Massachusetts Board of Registration in Medicine as the result of a conference that this Board had with Dr. Frank H. Lahey, chairman of the Procurement and Assignment Service, Dr. Reginald Fitz, Massachusetts chairman of this agency, Dr. George Leonard Schmidt, Dr. Roger I. Lee and the Secretary.

The proposition is briefly stated in a vote which was adopted by the Board of Registration in Medicine, on October 14, 1942.

Voted to ask the Governor of Massachusetts to waive the law (Chapter 112, Section 2, T. E.) to the effect that we may temporarily permit members of the medical profession, who are graduates of approved schools, who are registered to practice in other states and who are recommended by the National Procurement and Assignment Service, to practice in Massachusetts during the emergency without payment of the registration fee, and without examination.

This action on the part of the Board grew out of representations made by the National Procurement and Assignment Service, through its chairman, Dr. Frank H. Lahey.

This agency in these representations stated that its objectives were twofold: to supply the armed forces with physicians, dentists and veterinarians and at the same time to provide sufficient numbers of these groups to care properly for civilian needs.

These representations went on to speak of some of the difficulties with which the agency was meeting in maintaining adequate medical care for civilians in certain parts of our country. One of these had to do with such strictures laid down by state licensing laws as prohibited a physician licensed in one state from practicing his profession in another without first fulfilling all the requirements—examination and so forth—of the second state.

If certain parts of these laws might be modified or waived for the duration of the emergency, the job of procurement and assignment would to this extent be made easier.

Dr. H. Quimby Gallupe, secretary of the Massachusetts Board of Registration in Medicine, was present at the meeting of the committee. He explained that, when the action of the Board was called to Governor Saltonstall's attention, the latter expressed his willingness to use his wartime emergency powers in this direction provided the approval of the Massachusetts Medical Society was obtained.

It was unanimously voted by the Executive Committee to approve this act of the Massachusetts Board of Registration in Medicine.

The actual drawing up of such an act is the duty of the Attorney General. When this matter was placed before the latter, he advised against it because he could not be convinced of its need in Massachusetts at that time. He expressed himself, however, as without prejudice against the time when the need might arise in this state. He also spoke of the possibility of legislative enactment along these lines.

The Executive Committee has also given consideration to this latter course of action, particularly since the receipt by the Secretary on December 10, 1942, of a communication from the Federation of State Medical Boards, acting through its executive committee in joint conference with the Directing Board of Procurement and Assignment Service. This letter includes a draft of proposed legislation and a statement of certain principles which should govern it.

The Executive Committee, at this time, recommends adversely in the matter of seeking in Massachusetts legislative action to this end. It does so because it believes the Legislature is sure to ask the same question as did the Attorney General as to the need of modifying the law at the present time in this state and because a directive from the Governor, when and if such a need develops, is much the simpler approach.

The Executive Committee, acting on the recommendation of the Committee on Membership, has

(1) Retired the following fellows:

James Alfred, Brockton
William G. Curtis, Wollaston
Stephen R. Davis, Lynn
Charles Dudley, Kingston
Everett V. Hardwick, Milton
Charles H. Hare, Boston
John F. Jordan, Peabody
J. Herbert Libby, Weymouth
Robert G. Loring, Concord
Charles J. Spaid, Springfield
John J. Sullivan, Dorchester

(2) Restored the following physicians to fellowship provided all their obligations to the Society are discharged within one month:

Frederick W. Celce, Holyoke
Henry A. Dunphy, Palmer
Benoit W. Garneau, Fall River
Bert B. Hershenson, Brookline
Thomas H. Kenney, Northampton
Charles Liebman, Brookline
John J. Sullivan, Dorchester
David Zacks, Brookline

(3) Accepted the resignations of the following fellows:

Harold D. Chope, Brazil (with remission of dues)
Harold I. Gosline, Amarillo, Texas
Grosvenor B. Pearson, Pittsburgh, Pennsylvania
Harry A. Warren, Champaign, Illinois

The Executive Committee has reviewed the report of the Committee on Membership as it refers to a former member who was asked to resign and who now seeks restoration to fellowship. The Executive Committee recommends the adoption of this report.

The Executive Committee has reviewed the budget for 1943, presented by the Committee on Finance, and recommends its adoption.

The committee has reviewed the report of the Committee on Public Relations and recommends the adoption of its recommendation.

The committee has reviewed the report of the Committee on Medical Education, anent the nursing situation. It commends this report to the attention of the Council.

The committee reviewed the report of the Committee on Arrangements and approves the recommendations contained therein.

The President was in receipt of the following communication from Dr. Reginald Fitz, Massachusetts chairman of Procurement and Assignment Service:

Office of Defense Health and Welfare Services
Procurement and Assignment Service
Office of State Chairman
319 Longwood Avenue, Boston

December 7, 1942

Dr. George L. Schadt
44 Chestnut Street
Springfield, Massachusetts

Dear Dr. Schadt:

A curious finding has arisen which it seems to me deserves consideration. Approximately 1900 Massachusetts doctors (1942 *American Medical Directory*) have commissions or have had commissions with honorable discharge in one of the branches of the armed forces. Of these 1900, only 1050 are members of the Massachusetts Medical Society. Of the 850 commissioned officers who are not members of the Society, 200 in round numbers are substandard school graduates and not necessarily

desirable for the Society to worry about. That leaves a pool of about 650 young men who represent sort of a float ng medical populat on.

In th s pool are interns residents fellows jun or teachers in medical schools who come here for two or three years and such people. Potentially in normal times they represent a valuable part of our medical populat on because practically all are engaged in full time work or are active in research or teaching. I raise the quest on whether the Society and the Boston Medical Library might not make some effort to attract men of this type.

Could we not offer some sort of a jun or or temporary membership p to both organizat ons at a reduced fee and would it not be worth while for these organizat ons to stir themselves up in order to make the work as appealing as possible to men of this type? What is your thought on the matter?

As ever

REGINALD FITZ, M.D. Chairman
Massachusetts State Committee

The committee recommends that this matter be referred to the Committee on Membership.

The Secretary was in receipt of a telegram from Dr. Olin West, secretary of the American Medical Association, recommending the creation of a committee in the Massachusetts Medical Society to be known as a War Participation Committee. The committee recommends that the President be authorized to appoint a committee of five to serve this purpose.

The President was in receipt of a letter from Dr. Charles S. Butler, treasurer of the Massachusetts Medical Society, requesting an indefinite leave of absence because of ill health. The committee recommends that Dr. Butler's request be granted, that the Council express its great thanks for his fine service to our organization and its regret that he has found such a step necessary.

The committee approves of the recommendation of the Committee on Finance that Dr. Butler's salary be paid to him up to and including December 31, 1942.

The committee also approves of the recommendation of the Committee on Finance with regard to the figure set as compensation for the Treasurer *pro tempore*.

The President received the following letter:

December 30, 1942

Dr. George W. H. Schadt, President
Massachusetts Medical Society
Boston, Massachusetts

Re: Gift to Massachusetts Medical Society

Dear Doc:

Enclosed please find my check for \$1000 as a gift to the Massachusetts Medical Society to be used in carrying out its usual functions as an educational body.

I would suggest that—though I do not make a binding condition of the gift—it is I find be used to procure any necessary lunches for the official meetings of the Committee on Ethics and Discipline. I have in mind the many hours spent and the difficult problems dealt with not lastly at such meetings.

Please advise me whether the Society will accept this gift.

Sincerely

WILLIAM J. BRICKLEY, M.D.

The committee offers three recommendations with regard to this gift:

- (1) That it be accepted by the Council with thanks.
- (2) That it be used to create a fund which shall be known as the Dr. William J. Brickley Fund.
- (3) That it be used for the purpose outlined in Dr. Brickley's letter until otherwise ordered by the Council.

The President announced to the committee certain *ad interim* appointments. These appointments, which will be read later in the meeting, have the approval of the committee.

MICHAEL A. TIGHE, Secretary

APPENDIX NO. 6

REPORT OF THE COMMITTEE ON PUBLICATIONS

The committee has secured to deliver the Shattuck Lecture at the annual meeting of the Society in May, 1943, Dr. George W. Thorn Hersey, Professor of the Theory and Practice of Physics at Harvard University and physician-in-chief at the Peter Bent Brigham Hospital.

The committee has continued to supervise the publication of the *New England Journal of Medicine*. Under the able editorship of Dr. Robert N. Nye, the *Journal* has maintained its high quality as one of the leading medical publications in this country. The Society has reason to feel proud of the *Journal*. That the *Journal* is valued outside of the Society is evidenced by the increasing circulation among nonmembers.

We quote from Dr. Nye's report to the committee:

During 1942, the *New England Journal of Medicine* received 1984 new 'outside' subscriptions, a total that is over 50 per cent greater than the total received in 1941. Of these subscriptions, 1085 were from regular subscribers and 899 from medical students. As would be expected, there were many cancellations, undoubtedly owing to enlistment in the armed forces, the net increases were 216 regular subscribers and 711 medical students, which total 927. As of December 31, 1942, *Journals* were being sent to 5083 members of the Society (a decrease of 74 from the 1941 figure), 3462 regular subscribers and 1193 medical students, a total of 9738, which is greater by 853 than the total for 1941. This does not include 348 members of the New Hampshire Medical Society, who receive the *Journal* once a month.

The editorial board took action on 238 manuscripts during 1942, a decrease of 90 compared with the figure for 1941. Of these papers, 169, or 71 per cent, were accepted.

Operations for the year resulted in a net loss of \$17,550 which is approximately \$2450 less than the amount appropriated by the Society. The net cost per member of the Society was \$343, as compared with \$320 in 1941. There was an increase in operating expenses due to the larger circulation, the increased cost of binding and mailing, and the fact that in 1942 fifty-three issues of the *Journal* were distributed which happens every seven years, when January 1 falls on a Thursday.

It is difficult to predict what will happen in 1943. Undoubtedly the number of member subscribers will be decreased owing to their enlistment in the armed forces; on the other hand it seems likely that the number of outside subscribers will hold its own or possibly show a slight increase, in spite of cancellations. Expenses should decrease as a result of lower publication costs (provided the total circulation is smaller) and an increase in advertising revenue owing to higher rates which became effective on January 1. The decrease in the number of manuscripts submitted for publication may become a serious problem, in any event, the pagination of the *Journal* will be cut down, since the members of the editorial board believe that the high standards for acceptance should not be lowered. One typist, and probably two, must be added to the office staff, owing to the increased demands of the Society. This, however, will not increase the operating

costs of the *Journal*, since the Society pays for its share of expense.

An abstract of the auditor's report is attached as a part of the report of the committee.

JAMES P. O'HARE
CONRAD WESSELHOEFT
WILLIAM B. BREED
RICHARD M. SMITH, *Chairman*

* * *

New England Journal of Medicine

ACTUAL AND ESTIMATED FIGURES ON OPERATION

	ACTUAL 1941	ESTIMATED 1942	ACTUAL 1942	ESTIMATED 1943
REVENUE				
Advertising . . .	\$26,400	\$27,000	\$27,750	\$28,000
Engraving . . .	1,400	1,500	1,650	1,500
Reprints . . .	7,500	7,300	8,500	6,500
Subscriptions . .	20,400	21,000	22,450	24,500
Miscellaneous . .	800	800	800	800
	\$56,500	\$57,600	\$61,150	\$61,300
EXPENSE				
Publication of <i>Journal</i>	\$39,600	\$43,000	\$44,400	\$42,000
Publication of reprints	5,200	5,000	6,150	5,000
Office and other salaries	21,400	22,500	21,450	22,000
Commissions, fees and so forth	3,300	3,300	3 250	3,600
Office and sundry expense . .	3,500	3,500	3,450	3,500
	\$73,000	\$77,300	\$78,700	\$75,900
	56,500	57,600	61,150	61,300
LOSS . .	\$16,500	\$19,700	\$17,550	\$14,800
APPROPRIATION . .	\$20,500		\$20,000	\$15,000
BALANCE . .	4,000		2,450	
RETURNED TO M. M. S.*	3,100		900	
INCREASE IN CURRENT ASSETS	900		1,550	

*According to agreement with the Committee on Finance that the cash balance of the *Journal* shall not exceed \$6,000.

It is recommended by the Committee on Membership that the following recommendation from the then Committee on Membership passed by the Council on February 5, 1941, be revoked: "Fellows of the Society who are called to full-time service in the United States Army, Navy or Public Health Service during the present emergency and whose livelihood is thereby impaired may, on written application to the Treasurer stating their situation, have their dues remitted for the year of service. A period of full-time service greater than six months shall give the privilege of a year's remission of dues. The *New England Journal of Medicine* will be sent to such members only on payment of an annual fee of four dollars (\$4.00). The president of the Society shall determine the end of the present emergency."

The following recommendation in regard to members of the Massachusetts Medical Society is urged. "Fellows of the Massachusetts Medical Society who have enlisted or been called to full-time service in the United States armed forces or in the United States Public Health Service during this present war shall have no further dues collected for the duration, their names continued on the membership roll of the society as active members in good standing, and to only such members as request it will the *New England Journal of Medicine* be sent and then only on payment of an annual subscription fee of \$4.00 per year. Any members who have joined or who subsequently join the United States armed forces or the United States Public Health Service should advise personally or by some means the treasurer of the Society to facilitate omission of dues. 'For the duration' is interpreted as meaning honorable discharge from the United States armed forces or United States Public Health Service."

It is recommended that a flyer of this recommendation be attached to every bill or communication relating to indebtedness sent from the Treasurer's Office of the Massachusetts Medical Society to its members.

HARLAN F. NEWTON, *Chairman*

APPENDIX NO. 7

REPORT OF THE COMMITTEE ON MEMBERSHIP

The Committee on Membership, meeting with the supervising censors and in consultation with the Board of Membership of Suffolk District Medical Society together with the Committee on Ethics and Discipline, recommends that the application for reinstatement of Dr. Morris A. Cohen, 452 Beacon Street, Boston, this former fellow's resignation having been requested by the Committee on Ethics and Discipline, shall under the provisions of Chapter I, Section 11, be denied.

The Committee on Membership has received and carefully considered the nomination for honorary fellowship of Dr. Walter Fenno Dearborn by two fellows of the Middlesex South District Medical Society. Dr. Dearborn has gained renown through his achievements and research work in psychology and education at the University of Chicago, University of Wisconsin and now at Harvard University. As director of the Psycho-Educational Clinic of Harvard University he has made noteworthy advancements to arts and sciences and he is already famous for accelerating slow readers. Under the provisions of Chapter I, Section 4, of the by-laws, the Committee on Membership recommends to the Council that associate fellowship be conferred on Dr. Walter Fenno Dearborn, 79 Fresh Pond Parkway, Cambridge, because of his eminent work in the allied sciences.

APPENDIX NO. 8

REPORT OF THE MASSACHUSETTS COMMITTEE, PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS

Your committee has completed a year of active service under war conditions. During the year 1942, and up to January 15 of this year, 3743 Massachusetts physicians were classified. Massachusetts is credited with having 4366 doctors under forty-five years in age. Practically, therefore, most of our doctors of military age have now been examined by local Procurement and Assignment committees, and have been reported to the central committee in Washington as "available" for military service or "essential" to civilian needs. To accomplish such a task has been time consuming and has required hard work and great patience. Your committee is grateful to each member of each local committee for his assistance.

An analysis of our 3743 clearances brings out interesting information. A summary is as follows: 1477 commissioned in Army (39 per cent); 443 commissioned in Navy (12 per cent); 542 declared "essential" (14 per cent); 373 applied for commissions but rejected (10 per cent); and 908 declared "available" but have not applied for commissions (24 per cent).

It is believed that 2048 physicians from Massachusetts are now serving in the armed forces or have received

honorable discharge therefrom. For in addition to the 1920 officers cleared through your committee and commissioned, are the names of 128 physicians credited to Massachusetts by Washington who obtained commissions without clearance or whose clearance forms have been mislaid.

From time to time Massachusetts has been reprimanded for tardiness in filling its hypothetical quota of physicians needed for military use. The calculations involved in determining the quota are complicated. For example, a number of men listed in the *American Medical Directory* as belonging to Massachusetts may have Selective Service boards in other states, and, conversely, a number of young Massachusetts physicians with local boards here may have been at work outside of Massachusetts and may have been cleared through state committees elsewhere. The figures reported here deal with your committee's personal experience and with doctors listed as at work in Massachusetts according to the two latest directories. The committee believes that these figures illustrate the problem which Massachusetts faces. Each doctor on our records who is in the service has been withdrawn from the State and the position that he occupied in our civilian medical society must be filled by another or be done away with.

Either through letter or by personal interview we have heard from the majority of the 908 men declared available but who so far have not applied for commissions. A variety of reasons, each one logical enough, are brought forward by men who do not wish to volunteer: reasons of economy, or of a family nature, or because a man simply thinks that his talents at present are more useful to the community in which he lives than anywhere else. Your committee has attempted to deal with each case as fairly as possible. Every physician who has been interviewed has appeared to wish to do what is right and to determine this wisely has always been difficult.

From the 2293 men who were commissioned or who applied for commissions and were rejected, the following information has been tabulated: 1477 commissioned in Army (64 per cent), 443 commissioned in Navy (20 per cent), and 373 applied for commission but were rejected (16 per cent).

These figures demonstrate that in Massachusetts the ratio of Army to Navy commissions is about 3:1 and that our rejection rate is in the neighborhood of 16 per cent. Our relatively high rejection rate is due in part to the large number of graduates of substandard domestic schools or foreign schools who are licensed to practice in Massachusetts.

The substandard school problem was of considerable interest to the Society a year ago. An analysis of the fate of 200 such graduates who applied for commissions was made. Of these, 70 per cent were commissioned, 9 per cent were regarded as essential and 21 per cent were rejected. Of all Massachusetts physicians who have entered the armed forces, 11 per cent have been graduates of foreign or substandard domestic schools. It is obvious that the credentials of graduates of our domestic substandard schools and of foreign schools have been weighed carefully in Washington and that great care has been employed in deciding which applicants should receive the honor of a responsible post in the care of soldiers.

On many occasions during the year, your committee has been asked how many members of the Society were in active service. At the present moment (January 15, 1943) of 2048 Massachusetts physicians whom we believe

to have been commissioned, only 1122 (55 per cent) are members of the Society. This appears to be due to the fact that young doctors seem in no particular hurry to join the Society. Under ordinary circumstances Massachusetts has proved an admirable training ground and there is a floating medical population of young men who stay here for various lengths of time in some junior capacity. They have an intern's license to practice, they may take the

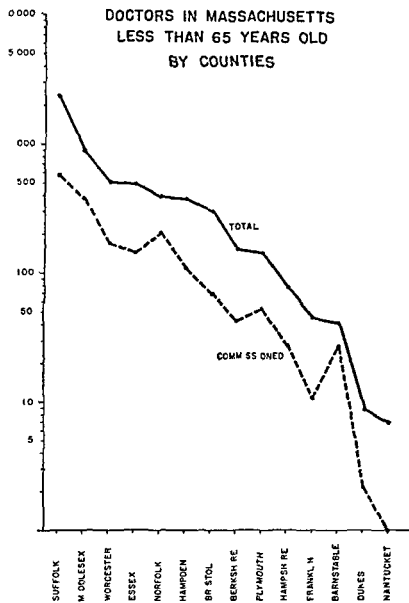


FIGURE 1

State Board examinations or they may have been certified by the National Board of Medical Examiners. Being uncertain as to where they will settle permanently, they do not take an interest in the affairs of the Massachusetts Medical Society, and besides, they are poor and busy, and have plenty of staff meetings and public lectures to attend. The committee hopes, when the war ends, that a method can be devised to attract such young men into some type of membership in the Society. They have users that are worth cultivating.

The experience of the year has been analyzed in a variety of ways in order to develop more detailed information by which to attack the work of 1943 with intelligence. Your committee has been informed by Dr. Lahey, that approximately 400 more doctors must be withdrawn from Massachusetts during 1943 to meet our quota. The type of doctor most urgently needed is the one who is young, preferably under thirty-eight years old.

On Figure 1, the solid line tabulates by counties the number of doctors who are less than sixty-five years old and the dotted line the number of men in each of the counties believed to be commissioned. On the whole, as

can be seen, all over the State there has been a striking parallelism in the ratio between the total number of doctors and those commissioned. Barnstable County appears to have been overgenerous, but otherwise each county

Finally, a chart has been constructed wherein is listed each town and city in the State, its population, its doctors, and the number commissioned, declared available, essential or unclassified. Of course the figures change

DOCTORS IN MASSACHUSETTS ACCORDING TO SIZE OF POPULATION

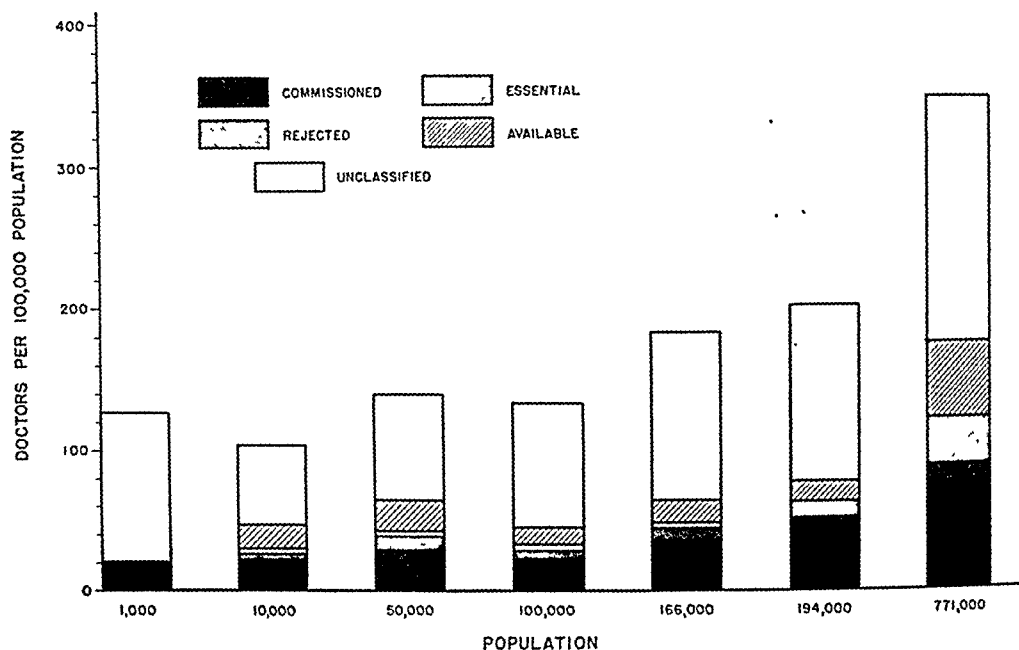


FIGURE 2.

appears to have given physicians to the armed forces in about equal proportions. This is a gratifying result.

It seemed of interest to study in greater detail the trends of medical population in cities of different size. With this idea in mind, cities of differing population were analyzed, the doctors of five cities in each group being averaged for those cities with a population up to 100,000; and for three larger cities, Springfield, Worcester and Boston were selected. In order to make results comparable, the physician numbers were expressed in numbers of doctors to 100,000 population. The doctors were broken down into "commissioned," "rejected," "essential," "available" and "unclassified" groupings. The resultant graph (Fig. 2) illustrates what appears to be a consistent trend: the larger the city, the greater in it is the concentration of medical talent. This fact is easily credible for in general the large city in a given locality has several hospitals, acts as consultant to the surrounding territory and thus, by necessity, requires more numerous and highly trained medical manpower than does the small city.

The chart illustrates another peculiarity with which the committee is familiar. The smaller the city, the more is taken as gospel the word "available"; the larger the city, the easier it is for "available" men to do nothing, unwilling to acknowledge that if they left, as Koko sang in the Mikado, "They'd none of 'em be miss'd."

On the other hand, if one takes the trouble to figure out proportions, the proportion of officers to doctors in the different cities is reasonably constant: areas thinly populated have not been allowed to become depopulated medically, except in rare and isolated instances.

from day to day, but the chart serves a useful purpose in helping your committee to visualize at a given time the ever-changing medical picture.

From all these data, it is possible to predict with reasonable accuracy, the fairest source of the 400 doctors who should be commissioned in 1943, taking into consideration population densities of cities and towns, and numbers of doctors. At this writing the most delinquent areas appear to lie in Suffolk, Berkshire, Essex and Hampden counties, with Barnstable too generous (Table 1). There

TABLE 1. Data on Physicians by Counties.

COUNTY	TOTAL PHYSICIANS UNDER 65	THEO- RETICAL QUOTA	PHYSICIANS COMMISS- SIONED	CREDIT OR DEBIT
Barnstable	42	17	28	+ 11
Berkshire	156	70	22	- 48
Bristol	302	110	96	- 14
Essex	499	200	153	- 47
Franklin	46	18	11	- 7
Hampden	379	152	126	- 26
Hampshire	79	32	30	- 2
Middlesex	898	383	367	- 16
Norfolk	398	207	209	+ 2
Plymouth	143	57	52	- 5
Suffolk	2332	882	643	- 239
Worcester	504	202	181	- 21

are various factors responsible for this, the most obvious one being the distribution of men who have applied for commissions but have been rejected. A man may apply for a commission and not receive it. It takes an appreciable time for this to be recorded and even longer for a man previously called "essential" to be declared "available" be-

cause a man previously 'available' has been rejected and thus is not liable to be taken out of the community. More over, interwoven with such a simple arithmetical problem in numbers is the more elusive one of quality. One well trained essential young man cannot be released even though ten imperfectly qualified physicians from his area apply for commissions and are found unacceptable to the Surgeon General.

If the table is actually filled according to this computation, each part of the State will do its proportionate share in sacrifice of medical care, there will be no depletion, and yet, the curve of doctor population ratio in cities of differing sizes shown in Figure 2—which the Common wealth has found satisfactory in times of peace—will be maintained.

It will not be an easy matter to procure the number of officers expected by Massachusetts in the next few months, for by now most of our young physicians wishing to obtain commissions have done so. On the other hand, Massachusetts is fortunate in having a large supply of doctors so that we can well afford to fill our quota and moreover, we are blessed with the heritage of patriotism.

H M CLUTE
E L KICKHAM
D O'HARA
W H PULSIFER
B P SWEENEY
R FITZ, *Chairman*

APPENDIX NO 9

REPORT OF THE COMMITTEE CONCERNED WITH PREPAYMENT MEDICAL CARE COSTS INSURANCE

I shall make a report of progress in regard to the Blue Shield.

The first matter concerns the enrollment of participating physicians. At the present time there are between 3300 and 3500 out of 4700 active physicians in the State who have enrolled. When I say 4700, that is an estimate of the men who are eligible to become participating physicians, excluding the men in the services, the men who are in institutions, the men who are in various state departments and the men who have retired. That figure is an estimate that I had from medical headquarters. So that gives a large percentage of participation.

This question of enrollment of physicians is directly related to the question of sales of the contracts, because the general rule through the country, on general medical care programs, is that it is not safe from the viewpoint of physician participation to begin local sales of the contract until there is at least 50 per cent participation by local physicians. Now, starting with our program, I think our problem is somewhat different. There is apparently need of satisfactory participation by the men to take care of the different services provided for in the first surgical obstetrical contract, in the various institutions in the districts. What delay has been encountered comes from trying to secure the enrollment of participating physicians so that all districts will be covered. A beginning of sales has been started in the Boston section because of the generous enrollment of the men there. Offhand it can be said I believe, that all the services are adequately covered in the hospitals in the main centers throughout the State.

There has been a request that local professional service committees and the salesmen (laymen) who will be re-

tive in trying to contact the many doctors who, said they will participate but have not yet signed. Their work can be facilitated greatly if that committee helps them in their approach to the members. They have lists of the men who have not yet sent in their contracts. They have a difficult problem because of gas rationing, which has been the main factor in delaying matters so far. Whatever help can be given locally will be greatly appreciated.

Just one last statement in regard to our approach to this matter on the basis of the partial-coverage contract. We have naturally been subjected to some criticism in getting our program launched with partial coverage rather than with complete medical-care coverage. That we may stabilize ourselves in this decision we have made, I quote two recent experiences that bear out the wisdom of this.

The first is that at a recent meeting at Chicago, where representatives of medical care plans met, one of the men, from California I believe, said that the approach through complete medical coverage was too idealistic. In Michigan they have definitely stated they have retreated entirely from complete coverage and are starting again on partial coverage. One of the northern New York plans, either Utica or Buffalo, has done the same thing.

I think an impressive thing regarding this matter is a recent announcement in the New York *Herald-Tribune* (January 11, 1943) from Health Group Cooperative, which is supported by funds from several of the large foundations. Their program, in effect, includes nothing more than surgical and obstetrical care in the hospital and home and medical care only in the hospital. In other words, those who comprised one of the major groups in criticizing the profession for not starting out with complete medical care have apparently had to retrench to the point where they leave out medical care in the home and office. From their experience they have found this a difficult problem to handle. I think coming from a group that so actively propagandized for complete medical care as an initial step, this fortifies us in our feeling that we were wise in our approach through a partial-coverage contract.

JAMES C. McCANN, *Chairman*

APPENDIX NO 10

REPORT OF THE COMMITTEE ON WAYS AND MEANS TO CONSERVE PHYSICIANS' ENERGIES

Perhaps a third of the able-bodied active practitioners of medicine are now withdrawn from their communities by the war effort. We freely accept this as in the interest of all the people. In some cities all physically fit doctors under forty-five have volunteered. We believe this will not seriously endanger the distribution of really essential medical care. In isolated instances attention has been focused on exceptions where community growth has mushroomed and it is not unnatural that the supply of replacement physicians lags behind the need. In some urban centers it is not yet apparent that there exists a present or potential shortage of doctors. In some of the medical periodicals reports of the measures adopted by organized medicine to adjust for shortage have been recorded. Some of the communities in Massachusetts have organized plans. Worcester has arranged for coverage of unmet needs for medical service from hospital centers. Each hospital has agreed to try to locate one of the doctors in its section on request. In Haverhill doctors have volunteered

to respond to night calls when the family physician (if there is one) is not able to comply. Physicians are listed for each night, a month in advance. The telephone office is co-operating. They know who is available for calls

PASTE THIS IN YOUR PHONE BOOK

SOON— Rationed Medical Care, Too

Haverhill doctors have responded well to the call from the armed services.

There are not as many able bodied younger doctors for the winter load.

Gasoline and tires must be conserved by the doctor, too.

A committee from the medical society is organizing the profession so that the essential quality of medical care will not be impaired.

Will YOU cooperate by:

Making no unnecessary calls?

Making your choice of a family physician and finding what are his office hours?

Calling his office between seven and eight in the morning when requesting house visits?

Being patient until he gets there? (Urgency of the illness and grouping calls by location must influence decision as to who comes first).

Giving your message to the office attendant unless you need to talk with the doctor personally?

Fevers are usually higher at night. If you postpone your decision to call the doctor until evening his capacity for service is impaired.

Arrangements will be made for someone to cover real needs at night.

FIGURE 1.

which come to them directly. This lessens the burden of potential nightwork and is patterned after the Army system of "officer of the day." Excellent co-operative spirit has been manifest.

The accompanying advertisement (Fig. 1) was published in the local paper and some physicians have had reprints with their own office hours appended. One of the local druggists has distributed reprints with his own endorsement.

We would like to call attention to commercial efforts toward public co-operation. Parke, Davis and Company, for example, have an excellent large display card, as well as folders to fit ordinary envelopes. These are dignified, well done and are available to all physicians.

We believe that the manner of handling the problem when and where it exists will vary with each community rather than with the district society. The medical profession in each community should assume responsibility for distribution of reasonably adequate medical care. This may well include institutional and nursing care as well as increased concern for public-health matters.

We believe that the Society can be a clearinghouse for new and better approaches. The American Medical Association has included this matter in its "Doctors at War"

radio series on a national hookup. We believe that local stations should be encouraged to include "Doctors at War" in their broadcasting programs as a public service. We believe that it may soon become desirable to co-operate with local stations for "flash" broadcasts of local conditions.

We believe that we should inform ourselves concerning and co-operate with hospitals', nurses', dentists' and druggists' adjustments to shrinking personnel and supply.

The matter of rationing hospital beds must be considered. We believe that hospitals can more effectively meet this problem by obtaining the assistance and co-operation of the staff in connection with admissions and demissions. This would demonstrate to the physicians so serving, and through them to the rest of the staff, their own obligation to censor potential admissions.

We like to believe that we have available an organization to apprehend and meet problems of distribution in medical care before they reach the stage of public indignation. Some newspapers have already indicated their belief that organized medicine has defaulted in this instance.

The Committee on Public Relations would seem to be an appropriate clearinghouse to initiate remedies. The chairman of the district committee is the delegate to the central committee. Most districts also have themselves subdivided by cities or community groups. This is highly desirable and we recommend your consideration of this plan of organization. In Essex North a special subcommittee was established in Haverhill for physicians. Another is organizing, with the nurses, a more effective adjustment to the serious shortage of nurses. In Worcester a special committee was established.

We recommend that the Committee on Public Relations be authorized to carry on the work for the Society.

ELMER S. BAGNALL, *Chairman*
CHARLES F. WILKINSKY
JOHN J. DUMPHY

APPENDIX NO. 11

LETTER FROM DR. HENRY M. LANDESMAN

February 2, 1943

Michael Tighe, M.D., Secretary
Massachusetts Medical Society Council
Boston, Massachusetts

Dear Mr. Secretary:

Enclosed please find two resolutions, being introduced in the General Court of the Commonwealth, for the approval by the Council.

One of these petitions deals with an arrangement for general reciprocity with other states, and to start immediate treatment when blood of an individual is positive.

The second petition deals with a plan to reduce the annual incidence of contagious and infectious diseases.

Sincerely yours,
HENRY M. LANDESMAN, M.D.

* * *

FURTHER REGULATING RECIPROCAL RELATIONS OF OTHER STATES IN REGARD TO FILING MARRIAGE INTENTIONS

Chapter two hundred and seven of the General Laws is hereby amended by inserting after section twenty B the following section:— *Section 20C.* A certificate of a

qualified or registered physician of any state whose laws are in substantial accordance with the laws of this commonwealth relative to the filing of marriage intentions, to the effect that such physician has examined one or both of the parties to the proposed marriage, that a serological blood test was made by an approved laboratory of that state, and that such test corresponds with that required by this commonwealth, shall be accepted as, and shall be, a sufficient certificate under the laws of this commonwealth.

When such serological blood test for syphilis is positive a clinical examination with subsequent checkup on blood test is positive the person involved shall be instructed to undergo treatment, either by a qualified physician who is competent to treat syphilis or by one of the clinics authorized by the laws of this Commonwealth and to continue such treatment until cured and discharged.

HENRY M LANDESMAN

PROVIDING A PLAN TO REDUCE THE ANNUAL INCIDENCE OF CONTAGIOUS AND INFECTIOUS DISEASES OF CHILDREN

Chapter one hundred and eleven of the General Laws is hereby amended by inserting after section ninety-one, as appearing in the Tercentenary Edition, the five following sections. Section 91A. It shall be the duty of every parent and guardian of a minor, whenever such minor is ill with any one or more of the following diseases, sore throat, common cold, grippe, measles, chicken pox, mumps, scarlet fever, whooping cough, chills or fever,

stiffness in neck, or rash on body, not to send such child or allow it to go to school unless and until it has been examined by a qualified physician or a physician of the local district board of health, whose duty shall be there upon to inform the parent or guardian that the condition of the child is either noncontagious or infectious, as the case may be.

Section 91B. The department of public health and the local boards of health of each political subdivision of the commonwealth shall respectively provide one or more physicians whose duty it shall be to visit children referred to in Section ninety-one A for the purpose of making diagnosis as to the possibility or probability of the infection or contagion to other children if exposed to the sick child.

Section 91C. Each teacher in each public or private school shall spend not less than five minutes in each school day in instructing the pupils under his charge in regard to covering mouths or noses while coughing or sneezing and as to the necessity of wearing proper clothing in cold or otherwise inclement weather and especially as to wearing rubbers in stormy or slushy weather.

Section 91E. Whoever violates any provisions of sections ninety-one A to ninety-one D, inclusive, shall be punished by a fine of not more than fifty dollars or by imprisonment in a jail or house of correction for not more than one month, or both.

Section 2. This act shall take effect upon its passage.

HENRY M LANDESMAN

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29111

PRESENTATION OF CASE

A twenty-two-year-old single shoe stitcher entered the hospital because of painful stiffness of the left side of the neck and weakness of this arm.

Approximately four months prior to admission the patient began to suffer with frequent brief attacks of burning pain in the left side of the neck and suprascapular region that radiated to the left shoulder, arm and thumb. The pain was exaggerated by movements of the head and seemed worse at night. During the periods of pain she noticed numbness and tingling in the left forearm and thumb and the left hand seemed cold and weak. Two months later she felt a swelling in the left side of the neck that seemed to vary slightly in size from day to day but did not apparently become larger.

The family history was noncontributory. At the age of six years an equinovarus deformity of the left foot was surgically corrected. For several years the patient had suffered with brief attacks of "stiff neck" that spontaneously cleared.

Physical examination disclosed a well-developed uncomfortable young woman who held her neck rigid, with the head turned slightly to the left. There was no atrophy of the scalenus or sternocleidomastoid muscles. The left longus colli muscle seemed atrophied. There was a slight dorsal cervical scoliosis, with the convexity to the right. Flexion and extension of the neck was good. The pain was marked in the midportion of the left side of the neck. The head could be bent to a 30° angle with the shoulder on the right and to a 55° angle on the left, and could be rotated 80° to the right and 60° to the left. There was tenderness along the left trapezius ridge, which was most marked in the region of a firm nonmovable mass that seemed to arise from the deep structures of the neck at the level of the transverse processes of the fourth and fifth cervical vertebrae. No pulsations were felt. There was hyperesthesia along the lateral aspect of the left arm and over the left shoulder. No loss of temperature, touch or vibration sense could be elicited. The left biceps and radial periosteal reflexes were absent. The plan-

tar responses were equivocally positive. Both hands perspired profusely. The pupils were equal and round. The diaphragm was percussed lower on the right than on the left. Examination of the



FIGURE 1.

heart, lungs and abdomen was negative, as was a pelvic examination.

The blood pressure was 104 systolic, 70 diastolic. The temperature was 98°F., the pulse 70 and the respirations 20.

Examination of the blood revealed a red-cell count of 5,300,000 with a hemoglobin of 13.6 gm. and a white-cell count of 6000 with 67 per cent polymorphonuclear leukocytes. The urine was normal. Repeated tests for the presence of Bence-Jones protein were negative. The blood Hinton test was negative. The serum calcium was 10.4 mg. per 100 cc., the phosphorus 4.0 mg., the phosphatase 2.2 Bodansky units, the protein 5.2 gm., and the albumin 3.7 gm. and the globulin 1.5 gm., giving an albumin-globulin ratio of 2.4. A spinal tap showed an initial pressure of 135 mm. of water. The dynamics of the fluid were normal, and it contained 1 lymphocyte and 14 red blood cells per cubic millimeter; the spinal-fluid protein was 29 mg. per 100 cc.

An x-ray film of the spine showed changes in the third, fourth and fifth vertebrae (Fig. 1). The articular processes and possibly the transverse processes of these three vertebrae formed one mass; the bodies and the greater part of the laminae and

spinous processes were destroyed by what seemed to be an expansile growth. An anteroposterior view of the lumbar spine showed no abnormalities. A chest plate was negative.

An operation was performed on the twenty-second hospital day.

DIFFERENTIAL DIAGNOSIS

DR W. JASON MIXTER: From the history we find a patient who had a lesion in the neck characterized by stiffness, by localized swelling and by pain, both locally and running down into the shoulder and the arm. The neck is a beautiful grab bag for almost any pathologic process, almost but perhaps not quite so good as the lower lumbar spine and sacrum. So far, however, there is little of diagnostic value. Although pain is usually absent in benign tumors of bone, this does not hold in cases involving the spine.

DR CHARLES C. SIMMONS: No, this is not bone pain but is caused by pressure on nerves.

DR MIXTER: Yes. Since the pain is due to nerve pressure, we cannot consider that pain is a diagnostic sign. Therefore, from the history alone we gather nothing except that the patient had a mass in the neck causing compression of the cervical plexus. Therefore, local examination simply confirms the impression that she had a tumor in its widest sense, in the cervical region. The fact that she could move her neck as well as she could tends to rule out an inflammatory condition or a malignant tumor, although not entirely. At any rate she had a tumor approximately at the level of the transverse processes of the fourth and fifth cervical vertebrae, with some loss of function in the arm.

The neurologic examination was not helpful. It suggests nerve compression. The plantar reflexes were equivocally positive. That is somewhat suggestive because then we begin to wonder whether she had spinal cord compression as well as compression of the nerve roots leaving the spine in the cervical region. Nothing is said about the knee jerks and ankle jerks or about clonus. I presume they were negative and absent, respectively.

DR TRACY B. MALLORY: I think it is safe to assume they were.

DR MIXTER: Repeated tests for Bence Jones protein were negative. At the same time we know that the absence of Bence Jones protein does not rule out the characteristic lesion that causes it. However, the serum calcium and various other blood constituents were normal so we come down to the lumbar puncture. We can probably rule out an inflammatory lesion on the basis of the spinal fluid findings, and I believe that the serum pro-

tein and other blood chemical findings rule out a widespread bone lesion.

The spinal fluid findings point away from compression of the spinal cord itself. The presence of one lymphocyte and fourteen red blood cells per cubic millimeter is unimportant and probably represents a slightly bloody tap. Therefore we can rule out an inflammatory lesion, probably including tuberculosis, and we come back to neoplasm.

The history suggests that it was of considerable duration because we find that for several years she had had brief attacks of stiff neck that had spontaneously cleared up. During the few months before entry, progression of the disease had been a good deal more rapid. So we come to the x-ray examination, which is of great value in lesions of the cervical spine.

DR RICHARD SCHATZKI: The record adequately describes the lesion. I do not see anything to add except that the process has led to marked shortening of the cervical spine.

DR MIXTER: Can you tell me which is the first dorsal vertebra?

DR SCHATZKI: Here is the first rib, this is the first dorsal vertebra.

DR MIXTER: In other words, the first, second, sixth and seventh vertebrae were normal. Hence, the lesion includes three vertebrae. Three vertebral bodies were thrown into one, with the spinous processes of the third and fourth fused together. There was certainly fusion of the spinous processes which points to a malformation, probably congenital. All that suggests that it had been going on a long time. There was a tumor on the left side of the neck, and the right side also appears to be involved.

We come down then to a lesion involving the bodies, the laminae and the spinous processes of three vertebrae. A lesion of that sort certainly suggests extremely slow growth and a congenital lesion, because that amount of fusion in the spinous processes usually occurs only in congenital lesions. We must also remember that the patient had a congenital anomaly of one foot. However, since the lesion increased rather rapidly during the years of early adult life, we cannot put it down as a purely congenital lesion of bone. Something else occurred that produced swelling and increasing pressure on the nerve roots. The lesions that I should think of in this connection are chordoma, giant-cell tumor and an enchondroma. There may be a good many others, but these three are the likeliest. I will put chordoma first.

DR MALLORY: Dr Schatzki, will you tell us how the argument ran in the X-ray Department?

DR SCHATZKI: I remember the case well and I believe that we said it was impossible to explain the whole thing by one lesion. The patient must have

had a congenital anomaly to account for the fusion of the three vertebrae, but that did not explain the expansile growth that the patient obviously had. The conclusion as I remember it was that she had two things, a congenital anomaly and an expansile growth; I believe we put giant-cell tumor first.

DR. MALLORY: Dr. Simmons, have you any comment?

DR. SIMMONS: I think Dr. Mixer has covered the situation well. My first thought would be a congenital anomaly because primary bone tumor rarely involves three adjacent bones. Destructive primary bone tumors have occurred in a few vertebrae, the commonest being the giant-cell tumor. I do not see how you can prove a chordoma. They usually occur at the extreme ends of the vertebral column.

DR. MALLORY: This is a possible situation for chordoma.

DR. SCHATZKI: Does it grow into the transverse processes?

DR. MIXER: I do not know that it does. I think that it could because one can see it growing into the bone at the base of the skull and out into the sides of the sacrum. There is no reason why it should not go out into the transverse processes. With all this destruction it may well be that your guess is better than mine; in other words, it may have been a giant-cell tumor.

DR. SIMMONS: In this hospital there have been several cases of giant-cell tumor in that situation.

DR. MIXER: To have congenital anomaly—I think all three of us are in agreement on that—and a neoplasm on top of it is an interesting combination.

CLINICAL DIAGNOSIS

Benign giant-cell tumor.

DR. MIXER'S DIAGNOSES

Congenital anomaly of cervical spine.

Chordoma?

Giant-cell tumor?

ANATOMICAL DIAGNOSIS

Benign giant-cell tumor.

PATHOLOGICAL DISCUSSION

DR. MALLORY: It was argued on the wards that one must assume both a congenital anomaly and a neoplastic process. For the latter, chordoma and benign giant-cell tumor were most generally considered.

The lesion was biopsied and showed giant-cell tumor. Subsequent to the biopsy a great deal of argument developed about whether the patient

should be treated by radiation, surgery or a combination of the two. The final consensus was to try radiation, which has been given in three courses with a considerable degree of improvement. The tumor mass has decreased significantly in size and the nerve-root pain seems to have disappeared entirely. On the other hand, the patient is not cured as yet; she is still coming back for treatment.

DR. MIXER: Since it was a giant-cell tumor I should like to ask Dr. Simmons how he would feel in a case of this sort about getting out as much of the tumor as possible and packing the tumor cavity with bone chips.

DR. SIMMONS: Following radiation a giant-cell tumor may be destroyed, but new bone is rarely laid down. The cavity is usually filled with fibrous tissue. The few cases that I have seen in which bone chips have been introduced have not formed new bone successfully. That is not true in an ordinary bone cyst.

CASE 29112

PRESENTATION OF CASE

First admission. A fifty-two-year-old single, former fisherman entered the hospital because of persistent burning epigastric pain.

Approximately twenty-five years before admission the patient began to suffer with occasional attacks of persistent burning epigastric pain, which was usually relieved by soda or food. These attacks occurred many times each year and lasted about a week but never interfered with his daily activities. Occasionally during an attack he belched a great deal, but he did not vomit. Seven years before entry, following the death of his mother, he was forced to live alone. Since then the attacks had occurred more often. A year before admission the pain became severer, and the patient gradually lost a great deal of weight and felt weak. He was seen in the Out Patient Department. At that time a healed, nonobstructing duodenal ulcer was demonstrated by x-ray studies. Ulcer diets partially relieved the discomfort, but the patient failed to gain weight.

The family history was noncontributory.

When thirty-two years old the patient had a sore on the glans penis, which healed promptly following topical treatment. Six years later both lower legs were amputated at the calf because of gangrene of the feet following frostbite.

Physical examination disclosed a markedly emaciated man who was nothing more than "skin and bones." However, he appeared to be comfortable. Examination of the heart, lungs and abdomen was negative.

The blood pressure was 88 systolic, 64 diastolic.

The examination of the blood revealed a red-cell count of 5,290,000 with a hemoglobin of 90 per cent, and a white-cell count of 7400 with 82 per cent polymorphonuclear leukocytes. The urine was normal. The blood Hinton test was negative. A stool was guaiac negative. A barium meal demonstrated a characteristic clover-leaf deformity in the duodenal cap but no crater was visible; the pylorus opened readily. A barium enema was negative.

The patient improved and gained weight on a high-vitamin, high-calory diet with supplementary iron, and was discharged on the thirty-third hospital day.

Final admission (six years later). The patient was readmitted because of sharp, crampy abdominal pain and constipation.

Following discharge the patient again suffered with epigastric burning pain, weakness and weight loss despite an adequate diet and rest in a convalescent home. Three and a half years later he began to worry about "people talking about him," and his abdominal pain seemed worse. Occasionally he became bloated and had slight heartburn when he ate small amounts of food. He never became distended and did not belch, but passed large amounts of flatus, which seemed to relieve him. Six months later a barium meal demonstrated that the duodenal cap was grossly deformed and that there was a shallow ulcer crater posteriorly; there was also some associated spasm of the first portion of the duodenum. The remainder of the examination was negative, as was a barium enema. The patient was treated with tincture of belladonna and a six-meal-a-day diet and seemed to improve. A gastrointestinal series four months later showed no definite evidence of activity in the crater of the duodenum.

Four days before entry he began to suffer with rather severe generalized abdominal cramps, which were most marked in the upper quadrants and were not relieved by food. These continued to the time of admission. He did not feel nauseated and did not vomit. Since the onset he had not moved his bowels or passed any gas, despite a desire to do both.

Physical examination revealed a mildly disoriented man. Examination of the heart and lungs was negative. The abdomen was moderately distended. There were generalized tenderness and spasm, but these were most marked over the lower abdomen. One observer demonstrated shifting dullness in the flank. The rectum was filled with firm impacted feces. The prostate was twice its

normal size, and was moderately tender and firm. No pelvic masses were felt, and no areas of tenderness were elicited.

The blood pressure was 72 systolic and 40 diastolic.

The red-cell count was 3,350,000, and the white-cell count 3500. The urine showed a +++ test for albumin.

A flat x-ray film of the abdomen showed marked dilatation of the sigmoid and a ground-glass appearance suggestive of free fluid. A small amount of barium inserted through the rectum passed to the rectosigmoid, where it appeared to be blocked; it was difficult to be certain of this, however, because the patient's relaxed anal sphincter permitted spilling of the barium.

Despite the administration of infusions of physiologic salt solution and glucose, blood transfusion and oxygen, the patient failed rapidly and died approximately sixteen hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD B. BENEDICT: This is a fairly obvious history of duodenal ulcer,—epigastric pain relieved by food,—and x-ray examinations on several occasions confirmed the diagnosis.

The sore on the glans penis is probably of no importance. It healed promptly, and later a Hinton test was negative. I cannot relate that to the gastrointestinal story.

The fact that he was down to "skin and bones" on the first admission makes one think of carcinoma, but since he recovered so rapidly and since his red-cell count was normal, such a diagnosis seems unlikely. Furthermore the patient was alive six years later.

Barium enemas were done several times and were consistently negative until the last admission, which may be of some significance.

The interesting part of the story is the acute episode that began four days before the final admission. The symptoms were then characterized by severe generalized cramps, mostly in the upper quadrants, and the patient had not moved his bowels or passed any gas. The question is whether he had a large-bowel obstruction with perforation or a perforated duodenal ulcer. Against a perforated duodenal ulcer is the fact that he had no sudden pain, as one would expect with a perforated ulcer, and there is no mention of any air under the diaphragm in the flat plate. He had an anemia, which would not be explained by a perforated ulcer, and a barium enema would probably not have been given if his attending physicians had thought the lesion was an acute perforated ulcer. The anemia certainly goes with a carcinoma of the sigmoid, and the x-ray findings were consistent with

a perforated carcinoma of the sigmoid. The white-cell count was low and cannot be explained by perforation unless the patient had an overwhelming infection, with no white-cell response. The temperature, pulse and respirations are not given.

From what I have read so far I am inclined to diagnose a duodenal ulcer and, in addition, a perforated carcinoma of the sigmoid. Will you show the x-ray films, Dr. Holmes?

DR. GEORGE W. HOLMES: Most of the x-ray films were taken at previous admissions. There is only one film taken at the last admission, and I am afraid that it is not going to help us. Apparently no film was taken at the time he spilled the enema. The films taken two years before the final admission were interpreted as negative, and I see no good reason to think differently. The only possibility is in the region of the cecum, but there is a good mucosal pattern all the way through and I am inclined to agree with the report. Of course there was plenty of time for something to have happened in the interval. In the last film there is a loop of dilated bowel on the left side, which appears to be large bowel. The bowel above it looks as if it contained fecal material. In other words, there is evidence of obstruction rather low in the large bowel, and nothing more.

DR. BENEDICT: How much weight do you put on the fact that the patient expelled an enema?

DR. HOLMES: If he had obstruction low down and was rather sick that is not an uncommon happening.

DR. BENEDICT: You think that he probably had obstruction?

DR. HOLMES: Yes. The only other explanation is that he was too sick to pay attention to what was going on.

DR. BENEDICT: I shall stick to my diagnosis.

DR. TRACY B. MALLORY: In view of the profound malnutrition, I doubt that the anemia was significant.

A PHYSICIAN: Was there any spinal-fluid test to rule out neurosyphilis?

DR. MALLORY: No. The opinion of the service was approximately that of Dr. Benedict. It was believed that the patient had large-bowel obstruction and that the duodenal ulcer was inactive.

CLINICAL DIAGNOSES

Volvulus of sigmoid, with perforation and peritonitis.

Perforated duodenal ulcer?

DR. BENEDICT'S DIAGNOSES

Duodenal ulcer.

Carcinoma of sigmoid, with perforation.

Peritonitis, general.

ANATOMICAL DIAGNOSES

Duodenal ulcer, with perforation.

Peritonitis, generalized.

Tuberculosis, healed, right apex.

Arteriosclerosis, generalized.

Amputation of both lower legs.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At autopsy we found a perforation, 0.5 cm. in diameter, of the duodenum through the base of a chronic ulcer. The large bowel was obstructed, but merely by fecal impaction, which was of impressive extent. There was, of course, a generalized peritonitis. Nothing else of significance was found. There was no evidence that he had ever had syphilis.

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AMERICAN RED CROSS

ALTHOUGH the collection of the blood for the 4,000,000 pints of plasma requested by the Army and Navy from the American Red Cross in 1943 is an undertaking whose difficulty and cost are readily appreciated not only by physicians but by the lay, this is merely one of the many useful and necessary functions related to the war effort that are being carried on by this organization. And of these functions, Home Service is an activity concerning which little is known.

Red Cross Home Service has been maintained for many years, and under peacetime conditions is an important cog in the machinery of disaster relief. Recent examples of this work in New

England include the aid given—and still being given—to families rendered destitute by the hurricane of 1938 and the care and help provided for persons involved in the Coconut Grove fire in Boston and for their families.

With the advent of war, the responsibilities of Home Service have increased manyfold. This is clearly evidenced by the fact that the personnel of this department of the Boston Metropolitan Chapter has increased from four in 1941 to one hundred and seventy five in 1943, with a corresponding increase in monthly budget from \$150 to \$6000. All this has been occasioned by various services to men in the armed forces—activities that are acknowledged by the Army and Navy to increase the fighting fitness of soldiers and sailors. The work, which is largely a co-operative effort of the Red Cross field service men at camps and at the front and the Home Service divisions at home, includes the following accurate information for the man who is worried about conditions in his home; the investigation of requests for emergency fur-
lough, with financial aid, if necessary, care for and assistance to the families of soldiers and sailors who have been killed or reported missing, and aid to former service men or their families in the filing of claims for relief funds or pensions.

This is part of the reason why the American Red Cross must raise \$125,000,000. It is part of the reason why the Boston Metropolitan Chapter must raise \$2,145,000, and why the suburban chapters must raise \$860,500 more. Surely no one can question the need for such a large sum of money, even though the drive comes at a time when the budgets of most families are in a precarious position. The men in the armed forces deserve all this, and more.

NATIONAL HEALTH ADVISORY COUNCIL

MOVEMENTS to improve the national health are numerous and familiar. But it cannot be expected that the health situation of the people will be per-

a perforated carcinoma of the sigmoid. The white-cell count was low and cannot be explained by perforation unless the patient had an overwhelming infection, with no white-cell response. The temperature, pulse and respirations are not given.

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the senior gas officers of defense councils in the organization of state and local programs. The senior gas officer trains gas reconnaissance agents who serve in the respective zones of their city. These men are responsible for the identification of the agent, the collection of samples, the prevention of casualties and the delimiting of gassed areas, and also for co-operation with Emergency Medical Service, the health department and other agencies concerned in protection against gas.

For Emergency Medical Service the duties are set forth as follows:

Duties before gas attack

- 1 Plan, with the assistance of the senior gas officer for the establishment of stations for the cleansing of gassed patients with other injuries and for the cleansing of civilian protection personnel. Each hospital of 150 beds or more should be provided with a cleansing station. Cleansing stations should be available in the ratio of one per 50,000 population and should be located at small hospitals or casualty stations if 150 bed hospitals are not available in this ratio.
- 2 Recruit, train and assign personnel to gas-cleansing stations for cleansing services.
- 3 Provide instruction, in co-operation with the senior gas officer, for general public and civilian protection personnel in self-protection and self-cleansing.
- 4 Provide for instruction of physicians in diagnosis and treatment of chemical casualties.
- 5 Assist hospitals in planning for the handling of gas casualties.
- 6 Assure adequate distribution of protective clothing and gas masks and other protective equipment to members of mobile medical teams and train personnel in their use.
- 7 Make provision for training drivers of ambulances and sitting-cars in the protection of their equipment against liquid gas contamination, inform them of arrangements for vehicle decontamination by Emergency Public Works Service.
- 8 Arrange for the protection from contamination of the equipment used to transport contaminated casualties in so far as it is possible.

Duties during gas attack

- 1 On advice of the senior gas officer and under the orders of the commander, man the gas cleansing stations.
- 2 Advise other services of the Office of Civilian Defense in regard to first aid cleansing of their personnel.
- 3 Assign a mobile medical team to gas cleansing stations for first aid.

Duties after gas attack

- 1 Evaluate the effectiveness of the cleansing procedures that have been used.
- 2 Provide follow up treatment of patients.
- 3 Prepare an inventory of protective equipment available for use in future attacks and obtain additional equipment as necessary.
- 4 Cleanse bodies of the dead to facilitate identification.

Gas masks are now being distributed to the personnel of the protective services.

Masks should be kept at the post where the protective personnel will assemble during drills or enemy action, not carried by them during their daily activities. It is recommended also that about 20 per cent of the masks allocated to each service be stored as a reserve. It is important that the reserves be decentralized as a safeguard against destruction by fire or bombing and also to permit rapid distribution in case of an emergency.

Since valuable and critical materials are used in the manufacture of gas masks, the utmost care must be exercised in their handling, distribution and storage. No person should receive a mask until he has been trained in its use and care, including proper storage.

Storage must be in a cool dry place, and masks should be kept from contact with sunlight, oils and corrosive liquids and vapors. After use, masks should not be worn by another individual without proper sterilization.

Repair of masks is not to be attempted locally except in case of extreme necessity. Broken and defective masks or those with exhausted canisters should be collected by the local property officer and returned to the supply depot for repair and replacement.

MISCELLANY

ARMY NAVY AWARD

TO PARKE, DAVIS AND COMPANY

The Army Navy pennant for excellence in production was awarded to Parke, Davis and Company, of Detroit on February 26. Brigadier General John M. Willis, commanding officer at Camp Grant, Illinois, presented the award which was received by Dr. A. W. Lescohier, president of the company. The insignia, which all employees are entitled to wear, were presented by Lieutenant J. B. Williams, senior medical officer of the Detroit Naval Armory, and were accepted by John Tighe, representing the employees.

NOTES

Dr. Ralph E. Wheeler, assistant professor of public health at Vanderbilt University, has been appointed professor of bacteriology at Tufts College Medical School. Dr. Wheeler graduated from Harvard Medical School in 1930 and received the degree of Doctor of Public Health from Johns Hopkins University in 1932. He will assume his new duties on April 1.

BOOK REVIEWS

Serology in Syphilis Control: Principles of sensitivity and specificity. By Reuben L. Kahn, M.S., D.Sc. 8°, cloth, 206 pp., with 35 tables and 1 chart. Baltimore: The Williams & Wilkins Company, 1942. \$3.00.

Hinton, Kahn and Kline have worked out precipitation tests in syphilis that are used on a large scale as supplements to or substitutes for the Wassermann reaction. These tests are being applied to millions. It is regrettable that quantitative procedures, such as Kahn discusses in one of the chapters of this monograph, have not had sufficient trial in practice, Wassermann, recognizing their importance, studied this problem for years. This book, however, does not deal primarily with the technique, but with the development, establishment and maintenance of sen-

sitivity and specificity levels of the tests, with special reference to the control of syphilis.

The role and limits of these tests are discussed in detail in the first four of the fourteen chapters; and their source is traced to the discoveries of the phenomena of complement fixation and precipitation in a survey that will be of interest to the historian of immunology. Although citing Neisser and Sachs as starters of the application of the Bordet-Gengou reaction to syphilis in his historical sketch occupying two chapters, the author does not quote the inspiring influence of Moreschi's phenomenon on their researches. A formula that takes into account the two main factors affecting the diagnostic value of serologic tests is the leitmotiv of the following chapters, in which the use of the supersensitive (presumptive) as well as of multiple tests is authoritatively discussed. The importance of standardization and the need of co-operation by syphilologists in carrying out this task are emphasized in a separate chapter. The first of the two chapters forming an appendix gives useful directions concerning the value of serologic tests for the control of syphilis by public-health officers. The summaries of fifteen papers presented at two conferences held in Ann Arbor bring to a close this interesting monograph.

The aim to give a fuller understanding of the principles of serology underlying the tests, without debating which one is the better or the poorer, has been properly achieved. The considerations brought forth by the author will enable the physician to best utilize these tests in the diagnosis and treatment, as well as in the control, of syphilis.

Intestinal Obstructions: A physiological and clinical consideration with emphasis on therapy. By Owen H. Wangenstein, M.D., Ph.D. Second edition. 4°, cloth, 484 pp., with 143 illustrations and 44 tables. Springfield, Illinois: Charles C Thomas, 1942. \$7.00.

It is only during the past decade that the complicated problems of intestinal obstruction have been attacked vigorously by the experimental method. No one figure stands out more prominently in the advances of this era than that of Wangenstein. Not only has he labored in the clinic and laboratory to find the answers to many of the unknowns of intestinal obstruction, but he has stimulated others to search for answers.

This book is a scholarly summary of the knowledge of intestinal obstruction to date. Many have associated the name of the author with the conservative treatment of intestinal obstruction. This is but a half-truth, and one need not read far into the book to discover that Wangenstein also operates for intestinal obstruction. The heading of one chapter is "Surgery: The mainstay of therapy." Cases of simple obstruction without strangulation can be safely treated by duodenal suction and the finesse of the surgeon lies in his ability to diagnose simple obstruction. Even Wangenstein seems to err on the side of operation when there is doubt of strangulation, but in the majority of cases he believes that a differentiation can be made on the basis of clinical and laboratory findings. The main thesis of the book, however, is not whether to operate. In spite of the author's personal experiences in this respect, he has risen above things close at hand and has given as impartial and comprehensive a review of intestinal obstruction as seems possible at the moment.

The physiology and pathology of intestinal obstruction are discussed in detail. At the end of the chapter "Effects of Distention," the author concludes that mechanical factors are far more significant than toxic factors in

explaining the effects of low intestinal obstruction. This essential clarification of a complex problem by a thorough rationalization of experimental data provides an eminently sound basis for all the therapeutic procedures that follow. The use of suction and its indications are reviewed. The surgical treatment of specific obstructions, such as intussusception, paralytic ileus and colonic obstruction, is given, with excellent drawings showing technic and pictures of illustrative cases. A lengthy bibliography follows each chapter.

Certain repetitions in the work are noticeable even when one reads through hurriedly. However, these are necessary to make a fairly complete unit of each chapter without resort to cross-reference. This feature makes the book a handy and readily available guide when specific problems concerning intestinal obstruction arise.

Psychotherapy in Medical Practice. By Maurice Levine, M.D. 8°, cloth, 320 pp. New York: The Macmillan Company, 1942. \$3.50.

This book gives in detail the various types of psychotherapy that can be applied in the treatment of the mental states, particularly the neuroses. The writer is a psychoanalyst and believes this is the best approach to the treatment of mental disorders. He does not, however, deny the limited value of the other forms of psychotherapy.

From the standpoint of the exposition of technic and the details of approach to patients, his book can be recommended as a useful addition to the general practitioner's library. From other standpoints, however, the reviewer finds much to criticize.

The familiar position of psychoanalysts — that they understand and can cure most of the mental difficulties of mankind — is well exemplified by the author. The psychiatrist knows all about the bringing-up of children, as well as being competent to advise in matters of marriage, sex, social relation, the choosing of a career and so forth, and the book provides a ready answer for difficulties, maladjustments and those mental illnesses concerning which psychiatry is, in reality, in a state of incomplete knowledge, to put the situation mildly. For example, the neuroses are not as yet understood either regarding genesis or regarding treatment, these fundamentals being quite unsatisfactory despite the claim of the psychoanalysts. Certainly the psychiatrist qua psychiatrist has not the wisdom, let alone the knowledge, to advise the human being successfully, beset as he is by the incongruities, cruelties and crudities of modern social structure, nor is there yet any ready reconciliation of the opposing forces to which every human being is subjected from the cradle to the grave. Psychotherapy of whatever form must yet prove its claims in the treatment of the major neuroses. It has contributed nothing of importance to the treatment of the psychoses, and it has remained for the physical approaches, such as shock treatment, to make an inroad on the grave problems presented by schizophrenia and manic-depressive psychosis. It seems safe to say that more concrete knowledge is to be expected from brain-wave studies than from any psychologic analysis yet evolved.

In the reviewer's opinion, extraordinary claims on the part of psychiatrists injure the growth and development of one of the most important and slowly developing branches of medicine. The psychiatrist has two main duties — to be humble in his claims and industrious in his researches.

(Notices on page xiii)

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THE BLOOD PRESSURE OF ADOLESCENTS Observations on Two Hundred and Twenty Students

HOMER E. LAWRENCE, M.D.*

BETHEL, MAINE

DURING the routine annual examination of 220 healthy male and female adolescent students, I was impressed with the frequency with which the blood-pressure readings reached elevated levels. In many cases, rapid pulse, excessive perspiration, vasomotor phenomena and other signs of excitement were absent. It was therefore decided to make further observations on these subjects, to compare the incidence of abnormal pressures with that in a group of young adults and, where possible, to obtain information regarding the blood pressures of the parents.

NORMAL BLOOD PRESSURES OF ADOLESCENTS

Before classifying a given blood-pressure reading as abnormal, it is necessary to know the normal reading for persons of the same sex and age. The blood pressure of adolescents should not be judged by adult standards. It has been pointed out that the blood pressures of normal children of the same age vary within wide limits, and that the normal value may be best described as a range.¹

The only studies of the blood pressure of sizable numbers of children available to me are those of Richey,¹ Faber and James,² Schnurman³ and Sundal.⁴ Sundal recorded only the systolic pressures obtained by the method of palpation. Schnurman did not observe persons below the age of seventeen. Faber and James did not record readings on adolescents older than sixteen. Consequently, the values given by Richey are the only ones suitable for the purpose of this study. The mean pressures and standard deviations recorded by him on students of the same age and racial stock as those observed in this study are given in Table 1.

In order to determine whether a given blood-pressure reading is normal, use is made of the statistical method of frequency distribution. This

method is explained by Faber and James² as follows. the nearer the pressure of a given subject is

TABLE 1 Blood Pressures and Standard Deviations in Adolescents (Richey').

AGE	NO OF CASES	MEAN SYSTOLIC		MEAN DIASTOLIC	
		PRESSURES	STANDARD DEVIATION	PRESSURES	STANDARD DEVIATION
		mm Hg	mm Hg	mm Hg	mm Hg
BOYS					
14	112	106.36±0.66	10.37±0.47	64.14±0.52	8.22±0.37
15	133	110.28±0.65	11.16±0.46	66.04±0.42	7.11±0.29
16	145	111.99±0.57	10.22±0.40	66.34±0.48	8.50±0.34
17	112	111.68±0.64	10.06±0.45	67.43±0.54	8.42±0.38
18	43	112.77±1.13	11.02±0.80	68.95±0.86	8.38±0.61
19	13	117.00±2.68	14.55±1.90	68.85±1.54	8.24±1.09
GIRLS					
14	115	103.94±0.65	10.27±0.46	67.10±0.48	7.65±0.34
15	121	105.88±0.63	10.31±0.45	67.43±0.45	7.36±0.32
16	128	106.69±0.63	10.53±0.44	69.09±0.45	7.50±0.32
17	97	102.96±0.63	9.94±0.48	66.88±0.54	7.53±0.36
18	34	100.53±1.18	10.22±0.48	66.41±1.05	9.06±0.74
19	7	104.71		66.43	

to the average of all normal persons, the greater is the chance that his pressure is normal; and the greater the deviation from the average, the greater the chance that his pressure is abnormal. The proportions are determined in the statistical system by the use of a measure of deviation from the mean, or average, which is known as the "standard deviation" (the square root of the arithmetical mean of the squares of the deviations from the average of the distribution). By dividing the deviation of a given measurement from the average by the standard deviation, one obtains a quotient, called by Faber and James the "deviation index." This index is of clinical value in determining the significance of individual variations

METHOD OF STUDY

The blood pressure of each student was taken at the time of his or her annual examination, a single reading being recorded. These readings were compared with Richey's¹ statistics for adoles-

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cents of the same sex and age. All subjects whose deviation indices were $+2.00$ or more were recalled for a second examination. This dividing deviation indices remained $+2.00$ or above, still further readings were made, including cold-pressor tests. In addition, information regarding the in-

TABLE 2. Data on 21 Subjects with Continued Blood Pressures of a Standard-Deviation Index of $+2.00$ or More.

CASE No.	SEX	AGE	RANGE OF BLOOD PRESSURE*	COLD PRESSOR TEST			BLOOD PRESSURES OF PARENTS
				BASAL	RESPONSE	TIME FOR RETURN TO BASAL RESPONSE	
		yr.	mm. Hg.	mm. Hg.	mm. Hg.	min.	
1	F	17	122-130/80-90	114/68	130/104	3	"No known hypertension"
2	F	15	120-150/70-80	118/70	134/100	3	"No known hypertension"
3	M	18	138-150/60-70	128/70	140/88	3	"No known hypertension"
4	M	17	136-152/76-98	128/80	146/104	2	"No known hypertension"
5	M	11	118-118/ 0-80	120/74	138/100	1	Father: hypertensive invalid Mother: pressure unknown
6	M	17	130-148/60-80	136/68	148/90	3	Father: pressure unknown Mother: 136/80
7	F	18	124-112/64-70	114/64	128/90	3	Father: pressure "slightly high" Mother: pressure unknown
8	M	19	130-140/80-86	120/70	134/98	3	Father: 130-180/80 Mother: 130/?
9	M	18	112-140/70-82	110/70	112/80	1	Father: 116/66 Mother: 142/76
10	F	17	136-142/76-80	130/80	144/90	2	Father: died of hypertension Mother: pressure unknown
11	F	17	122-140/68-80	138/80	140/98	1	Father: pressure unknown Mother: 136/66
12	F	18	122-142/68-80	126/82	136/90	2	Father: died of tuberculosis Mother: 158/76
13	F	16	118-132/72-74	114/70	130/100	3	"No known hypertension"
14	F	17	116-126/80-90	114/76	124/100	2	No information
15	F	17	126-144/70-84	112/60	130/90	1	Father: pressure unknown Mother: 148/84
16	F	18	130-150/68-80	130/70	130/84	1	Father: pressure unknown Mother: 138/84
17	F	15	126-142/58-80	112/78	126/90	4	Father: died of hypertension Mother: 162/90
18	M	17	134-152/72-76	130/70	140/110	4	Father: died of septicemia Mother: pressure unknown
19	M	14	130-140/68-78	124/70	134/98	2	Father: 130/80 Mother: 164/106
20	M	17	134-140/60-66	126/80	134/100	2	Father: 130/80 Mother: 170/100
21	M	15	150-158/70-80	148/80	162/90	1	Father: pressure unknown Mother: 180/100

*These figures indicate the lowest and highest values recorded in three or more observations some days or weeks apart; the readings are given in nearest even numbers.

line is purely arbitrary; so are the criteria for classifying adult pressures as normal or otherwise. It should be noted that a deviation index of $+2.00$ indicates that the odds against that reading's being normal are 1 to 43.² In a series of ideally distributed normal cases only 2.3 per cent will have indices of $+2.00$ or higher.

Blood-pressure readings were made by a standard method⁵ by one or both of two observers, whose readings were found in preliminary tests to check closely. Beginning with this second observation, the average of three or more readings was taken as the true reading. On the students whose

cidence of elevated blood pressure in the parents was sought.

RESULTS

Of the 220 students initially examined, 82, or 37 per cent, exhibited blood pressures whose deviation indices were $+2.00$ or more. Obviously, many of the elevated readings were due to excitement, although only 13 of the 82 subjects exhibited pulse rates of 90 or above. This was made further apparent by the second observation, when only 21, or 9.5 per cent of the entire series, continued to have elevations in blood pressure of this degree.

All the subjects had high systolic levels on more than one occasion. Cases 1, 9 and 14 had elevated diastolic levels as well. There is evidence that diastolic elevations are more significant than systolic.

The cold-pressor test was done on each of these 21 subjects according to the technic described by Hines.⁶ The subject was placed at rest in a reclining position in a quiet room, and the blood pressure was taken every ten minutes until a basal level was reached. The hand was then placed in ice water up to the wrist, and the blood pressure was read on the opposite arm after thirty seconds and after sixty seconds. The hand was then removed from the water, and readings were taken every minute until the basal level was regained. An abnormal response, according to Hines, consists of an elevation of 20 mm. or more in the systolic reading, an elevation of 15 mm. or more in the diastolic reading or failure to return to the basal level within two minutes. The diastolic response is said to be a more reliable index of vasoconstriction than the systolic. Among this group there were no students with excessive systolic responses. However, 16 of the 21 subjects, or 73 per cent of the entire series, showed diastolic responses of 15 mm. or more; and 10 of the 16 showed delay in returning to the basal level. This incidence of abnormal reactions should be compared with the 18.7 per cent incidence of hyper-reactors found by Hines⁷ among 400 school children.

BLOOD PRESSURES OF PARENTS

In 11 of the families of the 21 students with abnormally high pressures, the blood pressures of one or both parents were measured by me. In 5 couples, one parent had a systolic pressure greater than 150; and in 2 others, the systolic pressures were 142 and 148 in one of the parents. Furthermore, the husband of a hypertensive mother had died of hypertension. Unfortunately, it was impossible to observe any parent on more than one occasion.

The parents of 9 students gave what information they had by letter. One father had died of the complications of hypertension; the father of another was said to be a hypertensive invalid; and the father of still another had a "slightly high" blood pressure. There was no known hypertension in the remaining 6 couples.

Thus, in 20 couples concerning whom information was available, hypertension is known to be or to have been present in 7, and possibly in 10.

COMMENT

The incidence of hypertension among Selective Service registrants is said to be 3.02 per cent.⁸

Yet in the present study, the blood pressures of 21 of 220 adolescents, or 9.5 per cent, after repeated examinations were not considered normal. This may be explained in three ways: first, because Selective Service examiners do not determine abnormality by the method of frequency distribution, as was done in this group; secondly, because at least some examiners for the Selective Service System have subjects lie down if the initial reading is elevated, thus getting something comparable to the basal level of the cold-pressor test; and thirdly, because adolescents go through a period when they have elevated pressures that may become normal in young adult life, only to rise again to hypertensive levels in middle age.⁹

The hereditary aspects of hypertension have been pointed out repeatedly,^{7, 10-12} so that no comment on this aspect of the present study is needed here.

CONCLUSIONS

The drawing of definite conclusions regarding blood pressure from such a small number of observations is not in order. However, the following statements seem justified:

Blood-pressure determination should be part of the examination of students, but only if the readings can be checked at one or more later dates, for the pressures of adolescents are labile.

A certain proportion of students—9.5 per cent in this group—will show abnormally high pressures, as determined by the method of frequency distribution, after repeated observations. Most of these persons come from hypertensive families.

The frequency of abnormal pressor tests among these adolescents with abnormal pressures tends to confirm the impression that many of them are in a prehypertensive stage.

There is need for follow-up of subjects such as those described, in order to determine in later years whether elevated blood pressures and abnormal pressor tests during adolescence are truly indicative of a prehypertensive state.

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THE USE OF COAL TAR IN THE TREATMENT OF SKIN DISEASES*

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IN THE field of dermatology there probably exists no more valuable and useful remedy than crude coal tar. Nevertheless, no other substance in the *National Formulary* varies so in composition and consequently in pharmacologic action. This physical and chemical difference of coal tars derived from varied sources was originally emphasized by Dind,¹ who compared coal tars obtained from the gasworks of Lausanne, Geneva, Zurich and Basle. Brocq² recommended that one should insist on obtaining the coal tar produced in the making of illuminating gas. In these times it is impractical if not impossible to pursue such a policy. Many dermatologists when prescribing coal tar refer the patient to a certain pharmacist because the former knows the type of coal tar dispensed. If this is not practical, experience has shown that the patient not infrequently is given a mixture of uncertain composition, poorly compounded, which not only fails to benefit him but may be actually injurious. Furthermore, it is astonishing how often, when one prescribes *pix carbonis*, the pharmacist dispenses *liquor carbonis detergens*, a 20 per cent solution in an alcoholic soap-bark vehicle.

At the present day not only do the available coal tars differ from each other, but they all differ materially from that formerly recommended by Brocq, Jambon, Dind, Jadassohn and other European dermatologists. White,³ who introduced the use of coal tar in this country, was the first American dermatologist to mention this difference. Schamberg⁴ was so impressed with the unsatisfactory action and variability of the substance that he imported European tar for the use of his patients.

For a number of years at Bellevue Hospital, our experience has been similar to that in other sections of the country. Various lots of coal tar have differed in physical characteristics, color, consistence, homogeneity and therapeutic effect. On some occasions the substance used has been actually irri-

tating. This difference is due not only to the crude tar itself but also to the method by which the paste is compounded. It is extremely difficult to prepare by hand a good paste in large quantities. The finished product should be smooth, homogeneous and almost black. This shade does not differ perceptibly in pastes containing from 3 to 10 per cent of crude tar. Inferior and unsatisfactory pastes are sometimes an olive green, often flecked with small black particles, and lack the characteristic naphthalene-like, gassy odor.

What are the reasons for these differences in coal tars from different sources? The coal tar used by the early European dermatologists was the residue from anthracite coal in the manufacture of illuminating gas (*pix lithanthracis*). There were few uses for the crude tar, other than as a paint for wood, iron, rope, roofing, brickwork or stone as a protection against weather and fungi. It was subsequently distilled solely for the purpose of obtaining naphtha, creosote and phenol. In more recent years the value of coal-tar distillation fractions has assumed such importance in the arts and in industry that the manufacture of illuminating gas must be considered secondary. The separation of its constituents became an industry much more important than all the applications of crude coal tar itself. It was found that with variation in the temperature of the coal ovens, the time of distillation, the type of oven (vertical or horizontal) and so forth, differences occurred in the type of tar produced; that is, certain fractions were increased or decreased in amount. Coal tar was subsequently produced, therefore, of a composition depending on what fraction was particularly desired. This explains in part why many manufacturers use petroleum oil, coke, splint coal, lignite and other carbonaceous material, although the tar is medically more valuable when materials other than real coal have been used.

The only solution to the coal-tar problem appeared to be that a good crude product should be obtained and a competent manufacturer desig-

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nated to prepare a good paste. This was done, the product* consisting of the following ingredients:

Crude coal tar	2.88
Zinc oxide	5.37
Starch	53.75
Petrolatum, q. s. ad	100.00

METHOD OF APPLICATION

Detailed attention to the correct method of application and removal of coal-tar paste is essential to the best results.

All previous medication should be carefully removed by means of some fixed oil. The paste should then be applied directly by means of a wooden spatula in a layer just thick enough to cover the lesion. The entire area should then be dusted with talcum until the surface is white. If possible it is preferable not to cover the lesion with a dressing. If this cannot be avoided, the lightest type of dressing should suffice. The paste should remain undisturbed for at least twenty-four hours, and in some cases it may be left for two or three days.

Removal is best accomplished by using mineral oil or an emollient cream. No attempt should be made to cleanse the area completely; only the loose particles should be removed. A new layer of coal-tar paste is then applied in the manner previously described.

If papules appear on the treated area, the coal tar should be discontinued. They are the forerunners of pustules which may complicate therapy and are encouraged by too much bandage and a paste that is too thin.

Tar which has soiled linens and bedclothing may be readily removed by rubbing both sides of the material with lard and washing with soap and water.

The following precautions should be observed:

Avoid exposure to direct sunlight of the area to which tar is applied or has recently been applied. Tar is a photosensitizer, owing to the presence of acridine and anthracene oils.

Avoid prolonged use of tar on hairy areas. Folliculitis may occur, owing to pitch and paraffin oils.

Avoid changing the dressing often.

Do not apply tar to infected or impetiginized lesions.

Do not apply tar to more than one quarter of the body surface at one time. There is danger of absorption, since coal tars contain from 2 to 4 per cent phenol.

Be on the lookout for evidence of sensitivity after prolonged use.

Keep coal tar and coal-tar pastes in carefully sealed containers to avoid evaporation of volatile ingredients, which constitute a valuable part of their efficiency.

PHARMACOLOGIC ACTION

Since coal tar is not a uniform entity, its therapeutic action depends on the aggregate effect of its components. As these vary both qualitatively and quantitatively there must of necessity be minor variations in clinical effects between different samples of tar.

The antiseptic and antipruritic effects depend chiefly on naphthalene and the phenols and cresols. In a dilution of 0.1 per cent, tar exerts a definite astringent action.

The predominant effect of coal tar is keratoplastic, which is dependent on the presence of methylnaphthalene, dinaphthalene, xylenol and naphthol. Sulfur, which is present in a concentration of approximately 0.2 per cent, may contribute slightly to the keratoplastic action.

The reducing action of coal tar is closely related to its keratoplastic effect, and coal tar is exceeded in this respect only by dioxyanthranol, chrysarobin, pyrogallol and juniper tar. It has one distinct advantage over these substances: it can be used on vesicular lesions, which are invariably irritated by the other potent reducing agents.

The ability of coal tar to penetrate the epidermis depends on the presence of distillation products with high boiling points, especially methylnaphthalene. It abstracts oxygen from the skin, thereby inhibiting mitosis and resulting in a numerical and dimensional decrease in the cells of the rete malpighian and corneous layers.

CLINICAL USE

Infantile eczema. No single topical remedy is so beneficial in this condition as a properly prepared coal-tar paste. Those cases in which the face is covered with a crusted vesicular dermatitis are particularly amenable. The paste is applied in the usual way and a mask of soft light muslin or cotton cloth, fenestrated for the nose, mouth and eyes, is used to cover it. The dressings are changed not oftener than every twenty-four hours.

Occupational dermatitis, dermatitis venenata and contact dermatitis. These three dermatoses, which have certain features in common, are invariably benefited, whether they are vesicular or lichenified. With the multiplication of factories and new industries incident to the war, occupational dermatoses assume a new importance. The causative factors may be briefly classified as follows: mechanical irritants (dusts, sand, silicates, carborundum, duralumin, steel filings and so forth); inorganic

*The coal tar paste referred to is Daxalan, manufactured by Dome Chemicals Inc., of New York City; the tar is obtained from the Barrett Company Edgewater New Jersey

chemical irritants (soaps, soda, potash, lime, ammonia, mineral acids and so forth); organic chemical irritants (coal-tar derivatives, dyes, paints, plants and so forth); and mineral oils and greases. One precaution in the treatment of dermatoses due to contact substances is to avoid coal tar if there is much edema or any secondary infection. Cold, wet compresses of Burow's solution or boric acid should be used first to prepare the involved area for the coal-tar paste. Improvement is often dramatic and may be expected within a few days.

Dermatophytosis. Fungus infections of the feet and crotch, when vesicular, and vesicular dermatophytids of the hands respond well to the application of coal tar, although it exerts no direct lethal influence on the infectious agent.

Varicose eczema. Varicose eczema and varicose ulcers are promptly, although often only temporarily, improved by coal tar. In the absence of secondary infection there is no other agent that affords such rapid improvement.

Dermatitis hiemalis. By winter dermatitis is meant a condition characterized by more or less circumscribed, nummular and discoid areas of vesiculation, occurring in the winter, especially on the lower extremities, in individuals with a sluggish peripheral circulation, and accompanied by periodic pruritus. Response to coal-tar applications is good, although at times slower than in other vesicular eruptions. If the paste is applied sparingly and well covered with talcum powder, there is little soiling of the linen. Another method is to cover a thin coating of paste with flexible collodion or latex.

Chronic exudative lichenoid and discoid dermatitis, and dermatitis exfoliativa. Pruritus and cutaneous inflammations are greatly improved by coal-tar pastes. Depending on the cause, many patients obtain only temporary symptomatic relief. In all patients with generalized or universal involvement, it is advisable to limit the application to not more than one third of the body surface at one time.

Pityriasis capitis. Although the use of coal tar on the scalp is disagreeable, when the paste is mixed with an equal quantity of a fixed vegetable oil it may be conveniently applied by means of a toothbrush. No dusting powder is used.

Pruritus ani. The response of itching in the anal and perineal regions to coal tar is erratic. When there is an associated dermatitis with fissuring, the effects are better than those in essential pruritus. If improvement is not apparent within a week, treatment should be interrupted, since in this region folliculitis not infrequently compli-

cates tar therapy. In some cases favorable results are prompt and permanent.

Chronic dermatosis. The results obtained in prurigo, lichen simplex chronicus (neurodermatitis) and atopic eczema are frequently as good as those in acute conditions, although they are slower in attainment and often only temporary.

Psoriasis. The improvement following the application of a good coal-tar paste followed by ultraviolet radiation in ambulatory patients is often as good as those following the use of chrysarobin in hospitalized patients. The method used, essentially that suggested by Goeckerman,⁵ is as follows:

Remove all scales with green soap and water previous to instituting treatment.

Apply coal-tar paste to the lesions for twenty-four hours and then remove with mineral oil until only a slight brownish stain remains.

Administer mercury-vapor quartz-lamp exposures of just sufficient intensity to avoid a reaction.

Repeat this entire procedure daily, increasing exposures to produce tanning.

Permit the patient to take a bath after each exposure before reapplying the ointment.

Favorable results are frequently apparent within three or four weeks, although, as with other methods of treating psoriasis, they are seldom permanent.

SUMMARY

Differences in various coal tars, and in addition the methods of compounding coal-tar pastes, are responsible for variations in therapeutic response of various skin diseases.

Acquaintance with the physical, chemical and pharmacologic action of a coal-tar paste is essential for the best results.

When properly used, coal tar has a beneficial effect in a large group of acute and chronic inflammatory dermatoses.

The most satisfactory results follow the use of a paste of standard manufacture.

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CORNEAL TRANSPLANTATION

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THE subject of corneal transplantation or keratoplasty has become fairly familiar to ophthalmologists in recent years, and the operation itself is being done with increasing frequency. It should be even more important in the near future in military medicine, since a large number of eyes will undoubtedly be blinded from corneal scars due to traumatic injuries with infection or to burns. Since this operation is now a well-established and fairly successful medical procedure, it appears to be of interest to the profession at large.

Transplants are classified in two ways; by surface area and by depth. According to area, they are total if the entire width of the cornea is used, and circumscribed, or partial, if only a window is taken from the cornea. According to depth, they are lamellar when only the top layers or lamellae are replaced, and penetrating when the full thickness of the cornea is transplanted. Thus one recognizes four types of keratoplasty, total lamellar, circumscribed lamellar, total penetrating and circumscribed penetrating. Only the last one has a practical significance. Lamellar keratoplasty is a conservative procedure; but since a slight layer of scar tissue forms between the new and the old lamellae, it cannot give as good a visual result as a full-thickness, clear corneal graft. Total penetrating keratoplasty, involving replacement of the entire cornea, with or without some of the adjacent conjunctiva or sclera, has been tried many times, but the results have always been poor and have frequently necessitated subsequent enucleation.¹ Hence, the most popular operation at present is a circumscribed penetrating keratoplasty. In this procedure, windows 4 to 6 mm. wide are cut through the full thickness of the opaque cornea and replaced with pieces of clear corneas from enucleated eyes.

As with skin grafts, one also speaks of autotransplants (in the same individual), homotransplants (in the same species) and heterotransplants (between species, as from cat to man). The first and second appear to work equally satisfactorily, but heterotransplants, despite some temporary improvement, have never given a successful result in either man or animals.

Numerous methods of transplantation on both animals and human beings have been tried by many surgeons during the past hundred years, but only during the last two decades has clinical improve-

ment ceased to be regarded as a minor miracle. During the 1920's, Elschnig,² in Prague, and Filatow,³ in Odessa, did a large number of round transplants with trephines, with a few good results. In 1930, Thomas,⁴ in England, made an important contribution by beveling the edges of his trephine grafts. He⁵ has had many excellent results since that time. In 1932, Castrovicjo,⁶ in New York, published his first animal experiments, and since then he⁷ has made a greater number of important contributions to this subject, both clinically and experimentally, than any other ophthalmic surgeon.

The object of corneal transplantation is to restore sight to eyes blinded by opacities in the corneas. Unfortunately, not all such cases are suitable for operation. Favorable cases are those in which the eye is normal except for the cornea, the leukoma or scar is not dense or vascular; and there are areas of clear or slightly scarred cornea surrounding the graft to furnish it nutrition. Especially unfavorable cases are those with dense scarring of the entire cornea or with a vascularized pannus, such as that which comes from old trachoma. The eye can sometimes be rendered suitable for operation in the latter type by removing the pannus and using diathermy to seal the vessels at the corneal margin. Eyes with an old interstitial keratitis or conical cornea are unusually satisfactory cases for transplantation.

Another limiting factor in this field of surgery is the availability of donor eyes. Any enucleated eye with a clear cornea can be used. Such corneas are found in cases of intraocular tumor or blind and painful glaucomatous eyes where the cornea is edematous but has not yet degenerated. Eyes from newborn babies are also often used. Fresh material is best, but fair results are reported in eyes refrigerated for twenty-four hours.

Methods of operation are numerous. The most successful one is the graft developed by Castrovicjo.⁸ A square is cut two thirds of the way through the cornea with a double parallel-bladed knife. An oblique penetrating incision is made in the anterior chamber with a small triangular knife, or keratome, at the upper margin of this square. The square is then excised with special scissors, leaving the edges slightly beveled. The transplant is cut from the donor eye with the same knife and carefully slid into place from a flat spatula. The beveled edge on the host keeps this graft from getting lost in the anterior chamber, and several cleverly designed cross-stitches help prevent external dislocation.

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The circular graft of Thomas⁵ is also fairly satisfactory. A trephine hole is made two thirds of the way through the cornea, then continued at an angle so that an oblique penetration is made on one side. The cutting is completed with scissors, leaving a slight bevel. The graft is held in place with one vertical and one horizontal cross-stitch. Castroviejo⁷ has also perfected a modification of this method. Although I have never tried the Thomas stitch, I believe that the Castroviejo suturing is considerably more efficient.

Recently Wiener and Alvis⁹ introduced a method of cutting a slightly beveled graft with a corneal punch inserted through an incision near the corneal margin. This is by far the easiest procedure to carry out and the graft fits perfectly, but so few cases have been done by this method that its exact value is still unsettled. The peripheral incision probably does not hinder healing, but it leads to formation of anterior synechias or adhesions if a previous iridectomy has not been done. The synechias, of course, increase the danger of glaucoma. With this method, furthermore, unless the sutures are placed quite far out on the cornea it is easy to cut one when the bite is made; and if cut, a suture cannot safely be replaced.

Following operation, the patient is kept quiet in bed for ten to twelve days, and both eyes are covered for eighteen to twenty days. The pupil is kept dilated with atropine. The transient edema of the graft passes off during the first two or three weeks, and at the end of one month all but the periphery of the graft is clear and union is quite firm. Microscopic sections show conclusively that a successful graft retains its cellular identity and is not replaced by new tissue.

In unfavorable cases the graft usually takes, but soon becomes cloudy because of vascularization, proliferation of connective tissue on the back of the cornea or low-grade degenerative changes in the deep corneal layers, with loss of the normal parallel fiber arrangement there.

My own practical experience with keratoplasty has been limited to the last four years. The actual operation on human beings was approached in a rather guarded manner, with the result that up to the end of 1941 I had completed only 10 cases, one patient at that time having had a clear corneal graft for three and a half years. Because of this early caution, all these cases were classed as unfavorable in that they had dense or complete corneal scarring, vascularization or another ocular defect, such as former glaucoma or cataracts, nystagmus, chorioretinitis or extremely advanced and still active corneal dystrophy. The operation was also limited to eyes that had less than 5/200 visual

acuity and that, in addition, had a markedly defective companion eye.

The results were surprisingly good, however, since all grafts took, and all cases were improved (Fig. 1). The poorest result was in a case of vascularized and thickened complete leukoma of the cornea, which a keratoplastic surgeon in another city had refused to treat. The patient's vision six months after operation was limited to hand movements, but his original vision had been reduced to poor light projection with the ordinary flashlight, and he regarded himself as seeing considerably better. A patient treated recently also had a cataract, but it was thought best to do the transplantation first. As he has not yet had the cataract extraction, his vision is still poor; the graft, however, is crystal clear, so that the visual result will probably be good. The other cases have shown marked improvement, and several of the patients can read ordinary book print, including 2 patients with nystagmus and 2 with considerable myopia. Despite this ability to read, however, no patient has better than 20/70 vision.

These operations were done with the square graft of Castroviejo. More recently, however, I did my first punch-type transplantation. The graft took and was clear, but it had apparently slipped down slightly, leaving a tiny gap superiorly. This was the first time I had had any leakage from a wound. At the end of three weeks a conjunctival flap was put across the defect and at present it is still in situ. As the graft was transparent at the time of the flap, a satisfactory outcome is hoped for.

* * *

It is obvious from the work done in this field that corneal transplantation is a practical and not too dangerous operation. It seems best, however, to follow the custom already adopted elsewhere of operating on suitable cases with vision of 15/200 or less rather than selecting only the few extremely bad cases. As these corneas are more favorable to work on, future results may well include some normal or near-normal visual acuities.

9 Central Street

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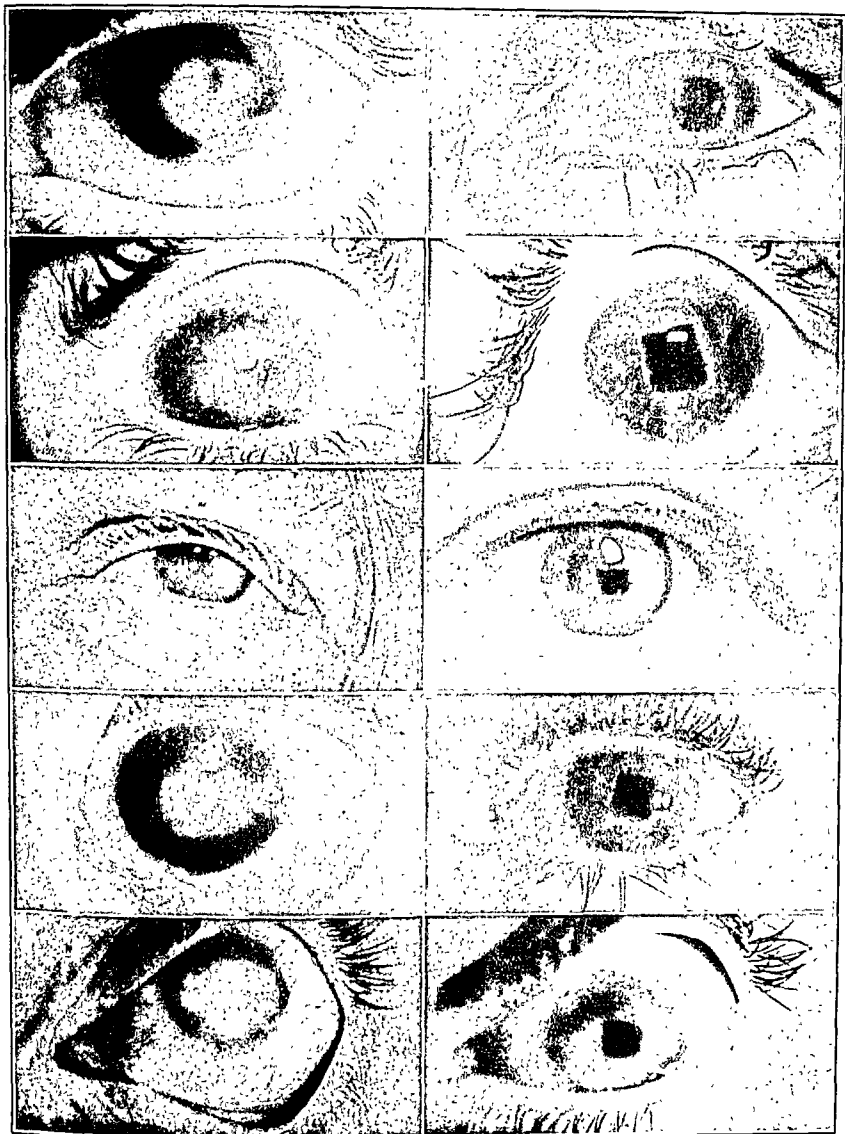


FIGURE 1.

Cases of Corneal Transplant Showing the Eyes of 5 Patients before and after Keratoplasty.

CLINICAL NOTE

PELLET IMPLANTATION*

THE SUBCUTANEOUS IMPLANTATION OF CRYSTALLINE PELLETS OF HORMONE

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SINCE the investigations of Deanesly and Parkes^{1, 2} on the subcutaneous implantation of crystals or compressed tablets (pellets) of androgens and estrogens, many papers have appeared in the literature describing this method of administering hormones of various types. These authors have shown that pellet implants are especially desirable when a prolonged steady effect is required, thus obviating the necessity of frequent injections of hormone over long periods of time. Using pellets of desoxycorticosterone acetate subcutaneously in adrenalectomized dogs and later in patients with Addison's disease, Thorn and his associates^{3, 4} reported excellent results and emphasized the advantages of administering hormone in pellet form. As a result of this advance in the treatment of certain hormonal deficiencies, a number of reports^{3, 5, 6} have appeared in the literature describing ways and means of facilitating the operative implantation of pellets of crystalline hormone subcutaneously.

This paper describes another operative technic that has been found successful in the subcutaneous implantation of pellets of desoxycorticosterone acetate in patients with adrenal insufficiency. It is believed that this procedure may be successfully employed to implant crystalline pellets of other hormones as well.

Implantation should be performed in the operating room under the usual aseptic precautions. The necessary instruments are simple and are found in most hospitals. The essential material is as follows: trocar and cannula (Fig. 1); glass rod; hypodermic syringe and needles; 1 per cent solution of novocain; scalpel; and suture material.

Experience has shown that this is best suited for patients. After a routine skin wheal is made with a long needle the

infrascapular region (Fig. 1A), an intracutaneous novocain block of the tissues is

infiltrated within an area of several centimeters. An incision about 1 cm. in length is made at the anesthetized site. A trocar with attached cannula

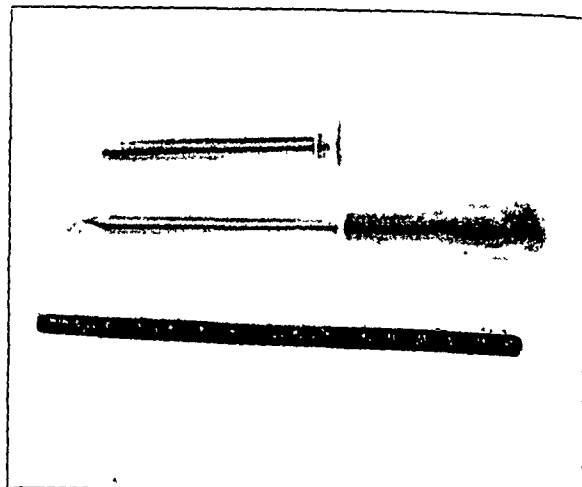


FIGURE 1. Photograph of Trocar and Cannula.

is easily introduced through the skin opening and gently forced into the subcutaneous tissue (Fig. 2B). The trocar is withdrawn, leaving the cannula in place (Fig. 2C). With forceps a pellet is

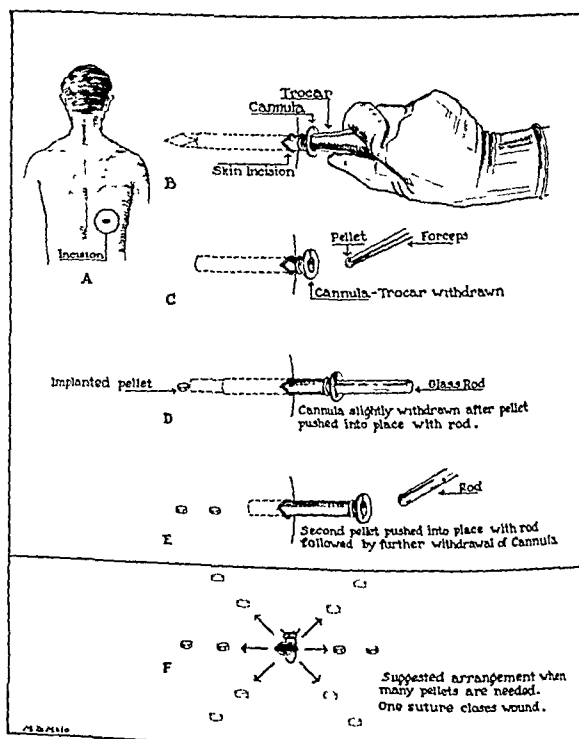


FIGURE 2.

ed into the lumen of the cannula and pushed into place with the aid of a glass rod (Fig. 2D). The pellet is held gently in place by the rod. The cannula is carefully withdrawn for about 15

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cm.* The glass rod is then completely removed and a second pellet is directed into place in a similar manner. The procedure may be repeated if a third pellet is to be implanted on the same side, but the operator should make certain that the cannula is withdrawn a short distance when each pellet is in place (Fig. 2E).

Following the implantation of one, two or more pellets on one side of the incision, the cannula is completely withdrawn. If more pellets are to be implanted, the trocar with cannula is inserted through the same skin opening but in the opposite direction, and the procedure is repeated. Should the patient's condition require inserting a large number of pellets, this is readily done by directing the trocar in other directions, always using the original incision (Fig. 2F). A single suture is all that is necessary to close the wound.

This procedure has many advantages. It has proved to be simple, short and effective. Trauma to the tissues is held at a minimum. Bleeding is negligible and hemostasis is not necessary. The gentle handling of pellets is assured; this is important, since crushing of one or more pellets may be harmful. Furthermore, since pellets are placed

several centimeters from the incision they are not easily extruded, as has occasionally been found to be true with other procedures. The clumping of pellets does not occur. Virtually any desired number of pellets may be implanted without difficulty. Likewise, the arrangement facilitates the location and removal of one or more pellets through a small incision should the occasion demand it.

SUMMARY

A simple, short operative technic has been described for the implantation of pellets of hormone under the skin with the aid of a trocar and cannula.

225 Carpenter Street

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*The outside of the cannula may be graduated in centimeters but this is really unnecessary

MEDICAL PROGRESS

THE USE OF DRUGS IN THE TREATMENT OF ASTHMA

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MANY articles have been written on the use of drugs in the treatment of asthma in the last few years, but there still seem to be difficulties and misunderstandings in various directions. It is consequently worth while to review the recent knowledge and to add one or two personal observations.

EPINEPHRINE (ADRENALIN)

When a patient is younger than thirty-five and the onset of asthma was before or about the age of twenty, the chances are good that the cause is not some pathologic lesion (intrinsic factor), but that it depends on a hypersensitiveness to a food, dust or drug in the environment (extrinsic factor). In such a case it is quite proper to inject a small dose

of epinephrine subcutaneously. If the attack is relieved, further doses can be given three, four or perhaps six times every twenty-four hours while the patient is at home. If, however, the asthma is severe and the doses of epinephrine have only a slight and transient effect, the patient should be removed to a hospital. The details of further treatment are relatively unimportant. Such patients will almost surely do well in the hospital, simply because they have escaped from the causative substance at home. The doctor should not be over-anxious to relieve the wheeze during the first few hours after admission. If the cause is a dust and the patient has escaped, the asthma will clear by itself. Also, the fatigue and anxiety which go with asthma will improve with the nursing care and the reassurance that are so important a part of the hospital management.

Epinephrine is the blood-pressure-raising constituent of the adrenal gland isolated by Abel¹ in

¹The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Series*, Volume III, 178 pp. Springfield, Ill., Charles C. Thomas Company, 1942, \$5.00).

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1897, and renamed "Adrenalin" by Takamine² a few years later. It is a sympathicomimetic substance the function of which is to stimulate the sympathetic nerves to make them overcome the action of the vagus nerves, which produce the asthma. In most cases the stimulation is effective, but if the drug is used repeatedly or given in too large doses, after a time the sympathetic nerves become overstimulated and the nerve-muscle cannot respond. The epinephrine is then said to have lost its effect.

The symptom asthma may be produced by a spasm of the smooth muscles in the bronchial wall, by a swelling of the mucous membrane or by an overactivity of the mucous glands. One or another of these results in a narrowing of the bronchial lumen and so in a wheeze. Whether the effect depends on a central and therefore a direct nerve stimulation or on the local action of some chemical effector substance like histamine or acetylcholine, which acts directly on the effector organ—the mucosa, the muscle or the glands—is still debatable, but the fact is that the result is a diffuse process which causes the signs of asthma to be fairly evenly distributed throughout the lung. In typical extrinsic asthma the signs are not limited to any one area.

Epinephrine is sometimes called on to stop the cough from bronchitis, with its mucus in the lumens of the bronchi, the dyspnea of heart disease, with its engorgement of pulmonary blood vessels, or the dyspnea of organic emphysema, with its dilatation and coalescence of terminal alveoli and its large spaces filled with air. But the drug cannot relieve these conditions: it is effective only when the symptoms are due to excessive vagal stimulation.

The dosage of epinephrine is important. When the correct dose is given to the right patient, the asthma is relieved, no new symptoms develop, and no harm results. When, however, too much epinephrine is used, the asthma itself may improve but the patient feels "queer." He turns pale and sweats slightly, the hands become cold, and the pulse becomes rapid and the heart pounds. There may be headache, and with all this a sense of weakness and collapse. In some ways the picture resembles that of surgical shock, but the blood pressure is usually higher, not lower, than normal. These side effects depend obviously on the stimulation of other parts of the sympathetic system. Thus, the heart is stimulated and the blood pressure rises; if continued, the effect may result in auricular fibrillation. As an example of severe reactions, a man of forty-two was seen at home on the third day of a severe asthmatic attack. His wife had given him epinephrine every 2 hours as

instructed, but the drug ceased to be effective. Unfortunately, the pallor, sweating and rapid pulse observed were not recognized as due to an excess of the drug, but were attributed to fatigue and loss of sleep. Still more epinephrine was injected. Within a few minutes the shock increased. The breathing became shallow, and the patient became almost unconscious. He was given $\frac{1}{4}$ gr. of morphine and hurried to the hospital. An intravenous infusion of 5 per cent glucose in physiologic saline solution was started and the patient rallied, his color and pulse returning to normal.

Such reactions from the injection of watery solutions of epinephrine are, however, infrequent. Keeney³ reports the case of a man of thirty-three who was given 0.5 cc. of a 1:1000 dilution by hypodermic injection. Violent headache with coma developed in a few seconds. The next day the patient had a right hemiplegia. He recovered slowly. The drug may have been injected intravenously by accident; many lesser reactions have come from that circumstance.

Three practical points are worthy of emphasis. In the first place, epinephrine is effective only when the patient's symptoms depend on spasm of the bronchial muscles or swelling of the bronchial mucosa. Secondly a small dose, that is, 0.25 cc., is usually quite as effective as a larger one. Patients vary in this regard, however, and it may happen that a given patient requires a large quantity. One should begin with a small dose and increase it gradually until the desired effect is obtained, after which it may be possible to reduce it. If the first dose is ineffective, a second may be injected in about fifteen minutes. Such pairs of doses, however, should not be given oftener than two hours apart. The intravenous injection of 1 liter of physiologic saline solution containing 1 cc. of a 1:1000 dilution of epinephrine is a useful procedure in cases of critical severity. And, finally, too much epinephrine does much more harm than good. If the patient has had repeated injections with no effect, the administration of further quantities may lead to serious difficulties.

High blood pressure is not a contraindication to the drug provided that bronchial spasm is present at the same time. When this bronchial spasm is relieved, the burden on the heart is lightened and the blood pressure goes down.

The effect of epinephrine appears within fifteen minutes. It may persist for many hours, but in most cases it lasts for not more than two to four hours. Efforts to prolong the effect have been made.

The administration of epinephrine in oil was suggested in 1938 by Keeney.⁴ The powdered base is suspended (not dissolved) in sterile peanut oil—

2 mg. per cubic centimeter or a 1:500 suspension. In Keeney's first experiment olive oil was used, but later he and his associates⁵ found that peanut oil was less irritating, since it contains less fatty acid. The usual dose is a whole ampule, or 1 cc. For some patients, the method is satisfactory, and the asthma is relieved for a longer period than it is by the ordinary watery solution. The fact that the speed with which relief of symptoms comes is about the same with oily as with watery epinephrine indicates that absorption at least begins promptly.

Reactions to epinephrine in oil, however, are not infrequent. In a recent paper, Keeney⁶ has reviewed them. Local reactions, consisting of redness, swelling and pain at the site of injection, depend on the presence of an irritating fatty acid in the oil or, more rarely, on an allergic response to the oil itself. More important are the systemic reactions. Symptoms of overdosage—pallor, palpitation and nervousness—not infrequently follow doses of oily epinephrine. Keeney reports 4 cases in which the symptoms were alarming. He points out that the large needle required for the oily mixture leads to rapid injection, and that the danger of placing the material in a blood vessel is greater than when the injection is given more slowly and through a smaller needle. Since in oil the epinephrine is present in a strength of 1:500 instead of 1:1000, one should be particularly careful not to inject the dose into a vein. Whether trouble comes because the epinephrine is a suspension of dry particles rather than a true solution Keeney considers doubtful. Dorwart⁷ reports the case of a woman of twenty-two with asthma who was given 0.3 cc. of 1:1000 aqueous epinephrine and at the same time 1.0 cc. of oily epinephrine. Within a few minutes there occurred shaking, pallor, twitching and cyanosis, with a pulse rate of 160, and the patient's condition became desperate. It was relieved temporarily by tourniquets, but she was not out of danger for five hours. More recently Maietta⁸ has reported that of 14 patients treated with epinephrine in oil, 2 had severe reactions. A man of thirty-seven with severe asthma was given 0.4 cc. of watery epinephrine and ten minutes later 1.0 cc. of epinephrine in oil. The effect was severe for one and a half hours. An obese woman of thirty-eight suffering from asthma of moderate severity was given only 0.4 cc. of epinephrine in oil. Within an hour came blanching at the site, followed by redness and swelling, which spread over the shoulder, arm and forearm. The local lesion lasted for six days.

Gelatin provides another medium for the administration of epinephrine, as Spain, Strauss and Fuchs⁹ have described. It is prepared by adding

one part of a 1:100 aqueous solution of the drug to four parts of an aqueous solution containing glycerin, sodium chloride, sodium bisulfite and chlorbutanol. At room temperature this solution gels, so that the ampule must be warmed before injection. The usual dose of 1 cc. contains 2.0 mg. of epinephrine. It can be given subcutaneously. In 50 cases the results were good and no untoward reactions were observed. Miller et al.¹⁰ have used epinephrine in gelatin in over 200 cases, and find it useful.

Epinephrine given as a spray to be inhaled directly into the bronchi was used first by Graesser and Rowe¹¹ in 1935. A relatively strong (1:100) dilution was employed—generally in a special fine nebulizer—and a large number of asthmatic patients were treated. If the bronchospasm was not severe, this method was found to be effective. Gagliani et al.¹² calculate that each squeeze of the bulb discharges only 0.008 mg. of epinephrine. Even so, they found that when rabbits and cats were given ten squeezes of this solution each day, after four months there was a loss of cilia and a desquamation of the tracheal and bronchial epithelium in some of the animals. Another slight risk is that the bottle of the former 1:100 epinephrine may be mistaken for that of the ordinary 1:1000 solution, and that a dose of the former may be injected subcutaneously. In one such case reported by Gormsen¹³ the patient died in a few minutes from a dose of 0.6 cc. (60 mg. of epinephrine) of the solution.

New products designed as substitutes for epinephrine have recently been reviewed by the Council on Pharmacy and Chemistry.¹⁴ Vaponefrin contains racemic epinephrine having the levorotatory and dextrorotatory isomers in equal parts (epinephrine *U.S.P.* is purely levorotatory). The dextrorotatory isomer is the much less active of the two, but analysis has shown that whereas the material as prepared contains 23 mg. of substance per cubic centimeter, it has a physiologic activity equivalent to that of 1:40 dilution of epinephrine. Vaponefrin is sold only to physicians, but products entirely similar are sold to the public under such trade names as Asthmanefrin, Neosol (also called Solution A or Inhalant A) and Nephron (also called Solution N or Inhalant N). Each of these is active and effective but expensive, as Barach and his assistants¹⁵ point out.

Epinephrine consists chemically of a benzol ring with two hydroxyl (OH) groups and a chain made up of two carbon and one nitrogen atoms. The hydroxyl groups on the ring make the compound unstable and give it optical activity. Further details concerning epinephrine appear in a comprehensive paper by Cori and Welch.¹⁶

EPHEDRINE

Ephedrine is closely related to epinephrine. It has no hydroxyl (OH) group in the benzene ring so that it is stable and is not optically active. The drug is useful in asthma; it is absorbed by mouth and controls mild bronchospasm. Its action is slow, and the dose, 20 to 40 mg. ($\frac{3}{8}$ to $\frac{3}{4}$ gr.), should be taken after supper if the effect is to be obtained at bedtime. Too much ephedrine may cause palpitation and tachycardia. The commonest difficulty, however, is that the drug causes sleeplessness, and on this account ephedrine has been mixed in various proportions with barbiturates and dispensed in capsules of many colors by different drug companies. Ephedrine is worth a try, perhaps, but if it does not control the symptoms, the patient should be given epinephrine, in place of forcing the dose of ephedrine to high levels. An interesting innovation is that of Brown,¹⁷ who coated ephedrine with a wax so as to delay its absorption for about three hours. By taking this tablet at bedtime, together with a dose of regular ephedrine, the patient receives a new dose of ephedrine automatically at about the time when the effect of the regular ephedrine is wearing off.

AMINOPHYLLINE

Aminophylline is a combination of theophylline with ethylene diamine. It was first used in 1937 by Herrmann and Aynesworth¹⁸ as a treatment for severe asthma. In the same year appeared a paper by Greene, Paul and Feller¹⁹ in which the drug was advised as a treatment for cardiac failure. These authors found that after the drug was given the breathing improved and the pressures in the vein and in the spinal fluid rose.

Theophylline is a xanthine derivative related to caffeine and to theobromine. All these drugs have a diuretic action, presumably because they improve the transport of fluid through the kidney capillaries. The addition of ethylene diamine to theophylline renders the mixture much more soluble, so that the combination called aminophylline is much more effective than is theophylline by itself.

In asthma the effect is good. Young and Gilbert²⁰ believe that aminophylline has a protective action against the bronchial constrictor effect of histamine. In guinea pigs, histamine shock and anaphylactic shock are both inhibited if the test dose is preceded immediately by an injection of aminophylline. So far, the mechanism that results in the relief of asthma by aminophylline is not clear.

Aminophylline must be given intravenously. If given subcutaneously it is much less effective, and furthermore it is irritating to the tissues. The dose

for intravenous injection to the average patient is 200 mg. ($3\frac{3}{8}$ gr.), which is dissolved in 10 cc. of water and comes prepared in ampules. A larger quantity, up to 400 mg., has been used, but is no more effective than the smaller dose.

Another preparation consists of 400 mg. dissolved in only 2 cc. of fluid. Supposedly this preparation is for intramuscular use. Occasionally, however, this concentrated material is given by vein; in such cases the patient has a sense of flushing and warmth, with palpitation and weakness, that may be quite troublesome. So far, severe and dangerous reactions following the use of aminophylline have not been described. Lamson and Bacon²¹ have used it freely, and even though their clinical description is long and complete, they say little about untoward effects. Incidentally, they find that the symptoms of hay fever and urticaria are improved by aminophylline quite as much as are the symptoms of asthma.

Aminophylline is prescribed in doses by mouth. The literature contains little about this topic, perhaps because the effect is hard to evaluate; certainly it is rarely striking. In the Allergy Clinic of the Massachusetts General Hospital, aminophylline is given in pills containing 0.2 gm. (3 gr.), to be taken three or four times a day. Several commercial preparations contain 2 gr. of theophylline in combination with $\frac{3}{8}$ gr. of ephedrine and $\frac{1}{8}$ gr. of phenobarbital. One in common use has 2 gr. of aminophylline in a similar mixture. Many patients declare that the ingestion of one, two or three of these tablets or capsules each day seems to protect them from their attacks. No doubt more are consumed than are really necessary.

WATER, SALT AND SUGAR

Almost all patients with severe symptoms that cannot be easily controlled should be given an intravenous injection of normal salt solution, usually containing 5 per cent glucose; a relatively large amount (1500 cc. or more) is allowed to run in with fair speed. In most cases the effect of this simple procedure is prompt and satisfactory. Patients with severe asthma cannot eat or drink. They have a tired, pinched expression, the tongue is parched, and they are dehydrated. To give such a person 1500 cc. of water containing 12 gm. of sodium chloride and 75 gm. of glucose helps very considerably. Sometimes improvement from this treatment begins promptly and develops dramatically when only 300 or 400 cc. has been run in.

The mechanism of this improvement is not at all clear. So far no studies of blood constituents or of the distribution of electrolytes have been made in asthma, and the field needs cultivation. Whether the addition of sugar accomplishes anything more

than providing a little food seems doubtful. In 1937 Wagner and Rackemann,²² among others, studied the glucose tolerance of patients with severe asthma, some of whom were in status asthmaticus, but found that the curve was like that for normal nonasthmatic subjects. The sugar metabolism in asthma appeared to be normal. Whether the injection of physiologic salt solution by itself without the addition of glucose is equally effective can be determined easily, but curiously it has not been tried in any series of cases.

Hypertonic glucose solutions have been advocated. In 1934 Lepak²³ at the Mayo Clinic treated 4 cases of severe asthma by injecting intravenously 100 cc. of 50 per cent glucose on each of two or three days and claimed good results. In 1938 Stoesser and Cook²⁴ gave similar treatment but in smaller doses to 3 children, and found that when the asthma was due to food allergy the attack was relieved, but when it was due to dusts the effect was not so good. Incidentally, children without associated pharyngitis and bronchitis responded better than did children with these secondary infections. In the same year Keeney²⁵ treated 6 patients with one or more intravenous injections of 100 cc. of 50 per cent sucrose (not glucose) to which had been added 0.5 cc. of a 1:1000 solution of adrenalin. In all, twelve injections were given, and with only two exceptions there was immediate relief from asthma, which lasted for at least two and a half hours. Stoesser and Cook²⁴ also used sucrose, but not with such good results.

OTHER DRUGS

Potassium salts. Potassium iodide has been described as the "sheet anchor" in the treatment of asthma. Most authors consider that its effect depends on its excretion into the bronchial tubes, where it irritates the mucous membrane and the mucous glands and so increases bronchial secretion. In this mechanism more stress has been laid on the iodine than on the potassium radical. Now, however, there is evidence that the potassium radical may be important. In 1938, Rusk and Kenamore²⁶ made the interesting observation that the injection of epinephrine causes an increase in the potassium concentration of the blood serum, and also that the intravenous injection of potassium salts relieves the symptoms of urticaria. Potassium lowers the irritability of the skin, making it less responsive to local irritation. Putting these facts together, the authors devised a "potassium regime." They made the diet low in sodium and high in potassium for the treatment of urticaria and of allergy. In the next year Rusk and his co-workers²⁷ found that potassium is stored in the tissue cells of the body, and that in allergy this store is depleted. Keys²⁸

found that after the giving of epinephrine the plasma potassium falls but returns to normal in about twenty minutes. Evidently epinephrine produces a change in the distribution of the potassium between cells and plasma. Since 1938 the use of potassium chloride has been discussed frequently, but unfortunately with no unanimity of opinion. Cohen²⁹ used the diet and the potassium chloride that Rusk and Kenamore advised, but saw no change in 8 patients. Bloom,³⁰ however, declared that it produced striking benefit in 29 cases of hay fever. Rusk himself gave potassium salts to 30 patients with hay fever, but with good effect in only 3 of them. Fürstenberg and Gay³¹ gave potassium chloride to 85 per cent of the patients in the clinic at Johns Hopkins Hospital, varying the doses and technic considerably, but the results were uniformly poor. Harsh and Donovan³² gave potassium chloride up to 18 gm. per day but were not at all satisfied that it did any good, for, as they point out, other factors could explain the small variations in the symptoms described. Obviously, there is much to learn about the physiology of allergy, especially of the asthmatic attack, and as said before, one can hope that accurate and complete data on the subject will be forthcoming.

Insulin. Bruhl³³ found that the intravenous injection of 10 units of insulin—he called it the "insulin thrust"—was useful in allergic skin disease, especially urticaria, and he tried the method in asthma, hay fever and mucous colitis. He is convinced that it is possible to influence allergic processes with insulin therapy. Insulin burns up sugar and lowers the blood-sugar level, and its effect is quite opposite to that of hypertonic glucose solutions. The results claimed for the "insulin thrust" make the problem even more confusing.

Sodium thiosulfate. The use of this drug is advocated by Klein³⁴ on the basis of some alteration in the body colloids. He has used it both by mouth and by vein in allergic epilepsy, in migraine and in urticaria, and declares that his results have been unusually excellent.

Amino acids. Tryptophan and histidine have been used by Lenormand,³⁵ who believes that they stimulate a hypersecretion of mucus, which in turn protects the hypersensitive membrane.

General anesthesia. It has been frequently observed that general anesthesia stops asthma temporarily. Perhaps this explains some of the beneficial results claimed for various operations that have been advised in the treatment of asthma. Anesthesia without operation has been tried; although this may provide temporary relief, the results are not so good as they are when some operation is combined with it. The prolonged

effect of the latter may depend on tissue injury, with the subsequent absorption of tissue-degradation products.

Ether. Ether in oil by rectum has been used occasionally. The results are satisfactory, and the mixture is not nearly so irritating to the bowel wall as one might expect. The dose is 30 cc. of ether and 30 cc. of olive oil, shaken well together and injected slowly into the rectum once, twice or even three times a day, if necessary.

Dilantin Sodium. This drug has been used as an anticonvulsant in epilepsy. Quite recently Shulman³⁶ gave Dilantin to 7 children with asthma in doses of 10 to 20 mg. (1½ to 3 gr.) per day and found the results good. The relief was maintained by continuing the drug in small doses once or twice a day. One must observe, however, that in children especially severe attacks of asthma are often followed by a remission, particularly if the patient is in a hospital.

Niacin (nicotinic acid). Maisel and Somkin³⁷ gave 100 mg. of niacin by intravenous injection to 20 patients with severe asthma. Sixteen of them were relieved within a few minutes. To 9 other patients doses of 200 mg. were given each day by mouth, and 5 were benefited. The use of this drug deserves further study.

Sulfonamides. The sulfonamide drugs have been used in asthma (Unger³⁸), and it is inevitable that many reports about them will be published. So far, however, the results are not encouraging, and the reason seems clear. Asthma does not depend on an acute infectious process. If bacteria are concerned, it is only because they have produced some chronic infection in the bronchi or nasal sinuses, and it is evident that the chronic process is always associated with pus. Since pus antagonizes the bacteriostatic action of the sulfonamides, in such cases the drug has little effect on the bacteria. To use sulfonamide drugs in asthma is like using epinephrine for heart disease: one is asking the drug to do something that it cannot do.

Histamine. The relation of histamine to allergy and asthma is always interesting. Dzsinich³⁹ first called attention to the treatment of allergic persons by giving them small doses of histamine. Little attention was paid to his work until Farmer and his co-workers⁴⁰ became interested in the clinical use of histamine. Histamine and acetylcholine are two substances that are normally present in the body tissues and are released by injuries to these tissues. Histamine comes from muscle and connective tissue, whereas acetylcholine comes from nerves. Together they are referred to as "cholinergic" substances. It is a temptation to consider them as the common denominators that give rise to the symptoms of hay fever and asthma,

a relatively uniform picture that is activated by a wide variety of exciting causes. To consider that asthma depends on an over-reaction to histamine or perhaps to an excess of histamine production is tempting, and so it is natural to consider the administration of histamine in an attempt to modify the natural reaction to it. So far the method is still experimental, and is not without danger, since histamine is a potent drug and doses above a certain limit are likely to cause reactions of considerable severity. Particularly in asthma, the treatment if given unwisely can easily precipitate an attack of great severity. The treatment gives some promise, but the details need careful study, and for the moment they had better be left to those who are thoroughly familiar with the drug and with the reactions that it produces.

Ether in oil from an ampule containing 1 cc. of ether and 1 cc. of peanut oil to be injected intramuscularly has been advocated by Maietta.⁴¹ Four patients with acute asthma were relieved by only one dose, and 2 others required two doses. In a group of patients who had had asthma for thirty or forty years, ether in oil given once or twice a week seemed to reduce the severity of the disease and to make other treatment more effective. And, finally, 2 patients with status asthmaticus were given ether in oil at intervals of 4 to 6 hours, with benefit. According to this first report the drug is useful.

DRUG ALLERGY

The literature on drug allergy is extensive, and part of it was reviewed in these columns in 1941.⁴² The symptoms are varied; they may be severe, and they appear when least expected. Three drugs are pertinent to the present discussion. *Aspirin* may be effective in asthma, but it should never be given without inquiring carefully whether the patient has ever had trouble from aspirin or other salicylates. Those patients sensitive to aspirin constitute a serious and difficult group. *Barbiturates* of all kinds are in a similar category. A hypersensitiveness to them may be present, and a pill taken to induce sleep—or, more important, a commercial preparation that contains phenobarbital—may not only fail to induce sleep in the patient, but may lead to a bad night for the doctor as well. The situation can become alarming. *Morphine* is important. I believe that it should never be used in asthma, although, in the case cited earlier I did give it when too much epinephrine had created a critical situation. Morphine is a cholinergic drug: it can actually cause bronchospasm. Furthermore, in severe asthma when the patient is gasping for breath, depression of the respiratory center may be the last straw. As the old darky said:

"Sam had the asthma powerful bad, but dat doctor is a great man. After he come, Sam he died jess so quiet."

* * *

From all this, it is quite clear that in asthma, as in other diseases, success in the use of drugs depends on the happy correlation of the physiologic mechanism of symptoms with the pharmacologic effects of the drug selected. To expect drugs to have an effect on a process that they cannot influence leads to discouragement, and some times to disaster.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29121

PRESENTATION OF CASE

A seventy-five-year-old Massachusetts-born farmer entered the hospital with the complaint of difficulty in swallowing of about ten years' duration.

Some fifteen years before entry he began to have "dyspepsia." This was characterized by slight pain in the "pit of his stomach" and much gas but no nausea or vomiting, and had no relation to the intake of food. An x-ray examination was alleged to have shown a "fallen stomach," and for some years the patient slept with his feet higher than his head, with apparent relief. About five years later he first noticed slight difficulty in swallowing large objects. Two years before entry he had great difficulty one day in swallowing a raisin, and only after an hour and the eating of considerable soft pudding did it finally slip along. Since that time solid food particles frequently stuck at a level that seemed to be slightly below the larynx. Ordinarily he was able to milk them down by rubbing his neck from above downward. No progression in the degree of obstruction was noted, although he ate only soft foods, until two days before entry, when he was completely unable to swallow a mouthful of custard pie. He had eaten nothing since then but had been able to swallow saliva and water. Throughout the ten-year period he had had no pain, nausea, regurgitation or vomiting. He had not lost weight and there had been no cough, hoarseness or change in character of the voice.

The family and marital histories were noncontributory. The patient had habitual constipation and had taken a phenolphthalein laxative daily for many years. For an unspecified period of many years he had been edentulous, and he had not recently used dentures because of soreness of his gums.

Physical examination showed a well-developed and well-nourished man with dry lips and skin. The gums were swollen, reddened and hypertrophic. No masses or tenderness could be made out in the neck. The lungs were normal. The cardiac apex impulse was neither seen nor felt

but the heart did not seem to be enlarged. The sounds were of good quality and there were no murmurs. The rhythm was regular. The abdomen was soft, without spasm or tenderness. One examiner recorded a questionable mass just below the xiphoid. There were bilateral, reducible inguinal hernias. The prostate was slightly enlarged but soft.

The blood pressure was 146 systolic, 92 diastolic. The temperature, pulse and respirations were normal.

Laboratory studies showed a urine with a specific gravity of 1.020 and no albumin or sugar. Blood examination showed a red-cell count of 4,300,000 with a hemoglobin of 78 per cent. The white count was 9500, and the differential showed 84 per cent polymorphonuclear leukocytes, without other noteworthy features. The blood protein was 6.3 gm. and the nonprotein nitrogen 20 mg. per 100 cc. The blood chlorides were 104.6 milliequiv. per liter.

Fluid barium taken by mouth filled the hypopharynx and upper 2.5 cm. of the esophagus, dilating the latter. The barium then met an obstruction at the level of the manubrium, and repeated efforts at deglutition failed to force barium past this point. Spot films showed a rounded collection of barium approximately 2.5 cm. in diameter above this point of obstruction.

The day after entry a biopsy was performed on the hypertrophic gum and an esophagoscopy was done. At the junction of the upper and middle thirds of the esophagus, 18 cm. from the anterior tooth line, an obstruction was encountered. There the mucous membrane was thrown into puckered folds but showed no break or ulceration. Soft bougies could be passed up to and including a No. 24. The esophagoscope did not pass. Several bits of tissue were taken for biopsy. Histologic examination of the two sets of specimens showed chronic gingivitis and no abnormality of the esophageal mucosa.

Following instrumentation the patient coughed up some "bloody pus" and thereafter found it easier to swallow liquids. On the fifth day a Beck-Jianu gastrostomy was done. Exploration of the upper abdominal cavity was negative. Following operation he seemed comfortable, and his temperature remained normal. The chest was clear except for a few moist rales at both bases. On the morning of the fourth postoperative day he complained of generalized discomfort which he was unable to localize. Examination showed slight abdominal distention, and the abdominal wound was found to have eviscerated to but not through the skin. The lips were cyanotic. The

blood pressure was 125 systolic, 80 diastolic, and the pulse 100. The heart and lung findings were unchanged. While being prepared for an enema the patient suddenly collapsed, became pulseless and deeply cyanotic, and expired.

DIFFERENTIAL DIAGNOSIS

DR. CARROLL C. MILLER: Cases of obstruction of the esophagus can be considered under three common headings: diverticulum, stricture and carcinoma. Benign tumors of the esophagus are relatively rare; malignant tumors are of fairly common occurrence as tumors of the gastrointestinal tract go. Strictures may be congenital but more frequently they are traumatic and usually due to the scarring caused by a caustic solution taken with suicidal intent or by accident. Carcinoma of the squamous-cell type is the usual malignant tumor.

We have here an elderly man with no symptoms of difficulty previous to ten years before he was first seen. At that time he began to have obstruction of the esophagus. The symptoms at the time of the first episode are a little confusing. It is said that he had "dyspepsia," which might be indigestion or perhaps heartburn or pain in the upper abdomen. He had slight pain in the pit of his stomach and considerable gas but no nausea or vomiting. Later on the record states that there had been no regurgitation or vomiting. I am unable to relate this particular symptom of dyspepsia to what subsequently developed, except by a referred influence on the motility of the stomach or encroachment on the wall of the stomach by some process above. I am not inclined to attach much significance to this symptom, except that perhaps it was the earliest, simplest sign of trouble higher up. Often, however, patients with tumor of the esophagus have no indigestion.

The x-ray diagnosis of "fallen stomach" probably has no significance, especially in light of the abdominal exploration that was done later. We are fortunate in being able to look back on the whole picture rather than part of it, as the original clinician had to do.

The question of esophageal diverticulum is an interesting and important one. There are some points about the case that strongly suggest a diverticulum of the esophagus. Diverticula occur in three parts of the esophagus, most frequently in the upper esophagus just below the hypopharynx. These are called pulsion or sometimes traction diverticula. The next commonest are in the middle half or upper middle third.

in the region of the bifurcation of the trachea, and finally but rarely they occur in the lower portion, where the muscle fibers start to thin out to become the cardia of the stomach. A patient with an esophageal diverticulum in the upper third often complains of something sticking at the region of the larynx. This may be due either to the lodgment of food particles in the entrance to the diverticulum or to filling of the diverticulum and compression of the esophagus, causing obstruction of the main lumen. A similarly significant symptom is the story of rubbing the neck from above downward to get rid of the food. This is frequently done by patients with diverticulum of the upper part of the esophagus. The pouch is low in the neck and by massaging that pouch the material contained therein can be expressed and deglutition can progress normally. We have no progression in this case for approximately two years. I assume that the patient was going on with the same general schedule of eating soft food, of massaging his neck and of having occasional bouts in which food stuck in the neck above the larynx; suddenly he became unable to swallow anything more than saliva and water.

On physical examination there were no clinical signs of a malignant process, and the x-ray findings were also negative. Patients with carcinoma of the esophagus frequently show loss of weight because of the difficulty in eating. We have no x-ray signs that could be called conclusive of carcinoma or tumor of the esophagus. The changes in the mouth—the red and swollen hypertrophic gums—were undoubtedly due to vitamin deficiency. This man probably was not getting his full quota of vitamins. He was living on liquids and a rather limited variety of them.

There were some rather interesting x-ray studies, and we might look at the films at this point. The barium taken by mouth filled the hypopharynx and the upper 25 cm. of the esophagus, dilating that part of the esophagus.

DR. RICHARD SCHATZKI: When one looks at the x-ray films there are a few things that may be added to the report in the record. One is the fact that the obstruction apparently was unusually complete. In none of these films do I see any barium beyond the plane of obstruction. Because of the marked obstruction there was some spilling of barium into the larynx and the trachea. The other point which may be added is that the round shadow is fairly smooth in outline but is irregular at the lower border in all the films, which may be due to tumor or may be due to food. I think from the evidence we have here it is impossible to say which of the two it is.

DR. MILLER: This pocket of barium is at the level of the manubrium as stated in the report, is it not?

DR. SCHATZKI: That is correct.

DR. MILLER: As I understand the topography of the esophagus that level is less than 18 cm. from the anterior tooth line as measured in esophagoscopy. Would that agree with the 18-cm. mark?

DR. RICHARD SWEET: I think it would agree, from the tooth line.

DR. MILLER: I had the impression that the obstruction seen by esophagoscopy was lower. Now I see that this is a well-rounded barium shadow.

DR. SCHATZKI: There is one lateral film, which may have significance. This is the filled hypopharynx, and you can see the round accumulation of barium about which we are talking. Between the two there is narrowing. It may be coincidental and transient, or it may be the neck of something. I do not know. You can see the same appearance in the anteroposterior view. On the other hand it seems to lie in the midline.

DR. MILLER: The fact that it lies in the midline is rather against a diverticulum because usually they are pressed to one side or they protrude from behind the esophagus so that they extend from the esophagus laterally. There was obviously some degree of dilatation of the esophagus from prolonged obstruction. The esophagoscopy showed an obstruction, which apparently extended all the way around the esophagus. I judge from the report that the esophagus was puckered and folded in its entire surface but showed no break or ulceration. An interesting fact is that bougies could be passed up to and including No. 24, which is a moderate size, thus showing that a certain amount of dilatation was possible, but not enough to allow the esophagoscope to pass.

The patient then had an episode indicative of sepsis. Bloody pus was coughed up, and at that point it was easier for the patient to swallow liquids. The medical attendants obviously thought that surgery was warranted, and exploration was done abdominally. Apparently no abnormal lymph nodes or no abnormality of the stomach itself was found, so a Beck-Jianu gastrostomy was done. For four days the patient seemed to do well but suddenly had a bad turn, the nature of which is indeterminate except for the fact that inspection of the abdominal dressing showed that he had an evisceration through the inner layers of the abdominal wall; then came a sudden collapse.

I have a feeling that this man must have had a carcinoma of the esophagus that perforated. The pouch seen in the x-ray film represents either an abscess cavity or a dilated esophagus above the

point of constriction, which Dr. Schatzki pointed out. The instrumentation of the esophagus stirred up the infective process in the abscess cavity so that the patient coughed up bloody pus, the product of the degeneration that had occurred there. The nature of the terminal episode I cannot be sure of, and it is not particularly important in the present diagnostic problem. It may have been a cerebral embolus, or it may have been a coronary attack. We have no data to indicate whether there were any symptoms of explosive cough which might indicate rupture of an abscess or tumor into the bronchial tree and cause the patient to become deeply cyanotic. Deep cyanosis can occur either with cerebral embolus or with sudden obstruction to the air passages. My diagnosis is carcinoma of the upper third of the esophagus with abscess formation.

DR. TRACY B. MALLORY: This case somewhat resembles a case you discussed recently, Dr. Lerman. How do you feel about this one?

DR. JACOB LERMAN: I am impressed by the fact that the x-ray films did not show irregularity of the esophageal wall, which is usually present with carcinoma of the esophagus.

DR. SCHATZKI: There is some irregularity.

DR. LERMAN: The description is not that of an ulcerative lesion. At least you did not mention it when you discussed it.

DR. SCHATZKI: It is irregular, however.

DR. LERMAN: Would you say it was ulcerated? The esophagoscopist did not describe ulceration. Since the two methods of examination seem to agree I should say that that is an important argument against it. Is there evidence of an extrinsic lesion pressing on the esophagus?

DR. SCHATZKI: None is visible.

CLINICAL DIAGNOSES

Carcinoma of esophagus.

Coronary occlusion?

DR. MILLER'S DIAGNOSIS

Carcinoma of the esophagus, with perforation and local abscess formation.

ANATOMICAL DIAGNOSES

(Cardiospasm.)

Esophagitis, acute, ulcerative.

Gastritis, acute, with pseudopolyposis.

Bronchopneumonia.

Pulmonary edema.

Pulmonary congestion.

Hydrothorax, bilateral.

Hydropericardium.

Cardiac hypertrophy, hypertensive type.

Arteriosclerosis, marked coronary and moderate aortic.

Nephritis, chronic vascular, slight.

Cortical cysts of kidney.

Operative incision: gastrostomy.

Incisional hernia.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The autopsy was done with the esophagoscopist present. He readily passed his instrument at the autopsy table, meeting no obstruction. On removing the esophagus we found that the first 1.5 cm. of the esophagus was normal. Below that point the wall was edematous and three or four shallow, apparently acute ulcerations were present in the esophageal mucosa. From there on down to the cardia the esophagus was markedly dilated and the wall extremely thickened, so that in spite of the fact that this story had from beginning to end suggested obstruction at the level of the larynx, all the anatomic evidence clearly points to chronic obstruction for many years at the level of the cardia. There was nothing anatomic to explain chronic obstruction in the upper part of the esophagus. It is an extremely odd story for cardiospasm, and yet that is the only diagnosis that is consistent with the anatomic findings.

DR. SCHATZKI: You assume that he had spasm in the region of the acute ulcer?

DR. MALLORY: The facts that during life the esophagoscope would not pass and that after death it passed easily indicate to my mind that the obstruction must have been spastic.

DR. LERMAN: The ulceration and gingivitis could be consistent with a deficiency syndrome.

DR. MALLORY: Yes. This is the second case we have had here in a month of benign ulceration accompanied by symptoms of stenosis in a patient with generalized vitamin deficiency. Since we published the first case¹ my attention has been called to a paper by Merrill and Richards² from the Pondville Hospital. They report three cases referred to the clinic as cases of carcinoma of the esophagus because of dysphagia, obstruction and even x-ray findings suggestive of carcinoma that were cured by intensive vitamin therapy. In these cases objective evidence of neuritis of the ninth and tenth cranial nerves was obtained.

DR. MILLER: Does this round x-ray shadow represent ulceration through the wall and a pocket behind it?

DR. MALLORY: No; the ulceration was only 1.0 mm. deep. This is simply localized dilatation above a point of stricture.

The terminal episode was massive pulmonary edema with a considerable grade of hydrothorax attributable to acute circulatory failure.

DR. SWEET: There are two points that ought to be mentioned in regard to this patient. On the wards we thought he had carcinoma.

We have learned in recent years the vast importance of a diagnosis of esophagitis. In our experience, it is much more frequent in the lower third or quarter near the cardia than higher up. I have run across it in the differential diagnosis of carcinoma several times, and it is a significant finding.

Furthermore, I have acquired this impression about biopsy. If the biopsy specimen shows only an inflammatory process with x-ray evidence that looks like carcinoma in the upper portion of the esophagus, the lesion is unlikely to be carcinoma. In the lower portion of the esophagus it is likely to be a carcinoma that has grown up from the stomach into the esophageal wall with a submucosal extension. In such cases the esophagoscopist may obtain only mucous membrane, the carcinoma lying deeper. I doubt if that happens commonly, although within two weeks we had a case in which an esophageal carcinoma opposite the manubrium was diagnosed with difficulty. The first biopsy showed chronic inflammation, and the second tumor. I have the impression that this discrepancy does not occur so frequently in high lesions as it does in lower ones, but we must be on the lookout for the diagnosis of esophagitis at any level. I have seen several cases.

DR. MALLORY: It is of great practical importance not to assume that a case of this sort has carcinoma of the esophagus and is therefore hopeless.

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CASE 29122

PRESENTATION OF CASE

An eighty-year-old retired grocer entered the hospital because of severe abdominal pain and constipation.

The patient was quite well until ten days before admission, when he became constipated despite the daily use of mineral oil. Five and a half days later he had two small bowel movements. The stools were brown but firmer than normal. Three days before entry he became slightly distended and developed generalized crampy abdominal pain. Several hours later he began to vomit a brownish fluid. The vomiting and pain continued unchanged to the time of admission. There was no pyuria, hematuria, chills, fever, jaundice, acholic, tarry or bloody stools.

The family history was noncontributory. For many years the patient had had an easily reducible left inguinal hernia, which a truss kept satisfactorily reduced.

Physical examination revealed a thin man who vomited frequently. The skin and mucous membranes were dry. The tongue was beefy red and dry. The chest was emphysematous, and the percussion note hyperresonant. A soft systolic murmur was audible at the apex. The abdomen was markedly distended, and the umbilical dimple flattened. Peristaltic waves were occasionally seen crossing the abdomen in the epigastrium and right lower quadrant. There was marked tympany over the entire abdomen. Only peristaltic rushes and loud borborygmi were audible, and these were loudest in the right half of the abdomen. There was generalized tenderness and rigidity. A large left direct inguinal hernia was easily reducible and was not tender. Rectal examination was not remarkable.

The blood pressure was 160 systolic, 75 diastolic. The temperature was 97.4°F., the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,400,000 with a hemoglobin of 70 per cent, and a white-cell count of 8100 with 62 per cent polymorphonuclear leukocytes. The urine was normal. A blood Hinton test was negative. A roentgenogram showed that the abdomen was filled with gas-distended loops of small bowel; one loop in the pelvis had somewhat the appearance of sigmoid. The only air in the colon seemed to be in the rectum, which was not distended. Several hours after admission a barium enema readily filled the large bowel and revealed no abnormality.

Parenteral glucose and saline infusions and citrated-blood transfusions were administered, and a Miller-Abbott tube passed. The latter passed to the cecum and decompressed the dilated loops of small intestine.

On the ninth hospital day the Miller-Abbott tube was pulled back from the cecum for about 30 cm. into the ileum. Barium that was passed through the Miller-Abbott tube showed a slightly but definitely dilated ileum. There was a sudden narrowing of the ileum beginning about 15 cm. proximal to the ileocecal valve, and there was marked peristalsis of the ileum proximal to the point of narrowing. The amount of barium pushed through the terminal ileum was small, but the greater part of this portion of the ileum was seen to widen out at one time or another. An area approximately 2.5 cm. in length at the beginning of the narrowed ileum never showed distention; the mucosa in this area seemed to be preserved.

There was a similar area closer to the ileocecal valve, which showed some rigidity.

An operation was performed on the tenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: May we see the x-ray films? Be very careful what you say, Dr. Holmes, because a great deal depends on you.

DR. GEORGE W. HOLMES: This is the type of problem where the man who did the examination had a much better chance than I have. Furthermore, it is the type of case that the radiologist needs about an hour's study before making any real statement. I am saying this so that I will not mislead you, because anything I say will probably be wrong. There are, however, a few things that are obvious.

At the time the barium enema was given, the patient had a tremendously dilated small bowel and some gas in the large bowel; it does not look as if he had any gross pathology in the large bowel. I think we can agree with the man who made the examination that the lesion was low in the small bowel and close to the cecum. His description is rather better than anything that I can give you.

DR. MCKITTRICK: The cecum is normal?

DR. HOLMES: Yes. So far as I can tell the lesion was in the terminal ileum or outside the bowel involving the cecum, such as an appendiceal abscess.

I am surprised that the Miller-Abbott tube did not deflate the bowel. Even with the tube in place there was still a good deal of gas. They took a film of the chest, which I should say was normal for a man of his age.

DR. MCKITTRICK: We must start with the supposition or premise that this man had small-bowel obstruction. I do not believe it is possible to have the amount of dilated small bowel he had from a lesion in the large bowel, and in addition to that we have the confirmation that was given by the passage of barium from the rectum to the cecum, which showed a normal large bowel. Therefore we start with the premise that this man of eighty entered the hospital with small bowel obstruction. That may not be correct, but it is the only diagnosis we have any right to make.

If we start with the argument that he had small-bowel obstruction, what was the cause? I am perfectly frank to confess that I can talk myself out of any diagnosis that I wish to make. The only evidence we have is that the obstruction was in the terminal ileum. That is all right so far. Then the problem is, What was the nature of this man's obstruction? It seems to me there are a

couple of ways of approaching it. He could have had intrinsic cause of obstruction, that is, a tumor or an inflammatory lesion. If it was a tumor, it was probably either a carcinoma, a lymphoma or possibly a leiomyosarcoma; if it was an inflammatory lesion, it was probably either tuberculosis or enteritis. The only other intrinsic type of lesion is foreign body, and I do not think we need give much time to that. If it was not intrinsic, and I do not believe that we can say definitely that it was intrinsic, then it could have been extrinsic, as Dr. Holmes has said. The likeliest extrinsic lesions are an inflammatory process, such as appendiceal abscess, an adhesive band, the most frequent cause of acute small-bowel obstruction, and a tumor in an adjacent structure pressing from outside. It seems to me that somewhere in that list is the explanation for this man's disease.

Let us consider an adhesive band, which is the most frequent cause of obstruction. I shall be greatly disappointed if he had such a lesion. From the history, if it is correct, the first symptom he had was constipation. No one with acute small-bowel obstruction due to an adhesive band has a right to have constipation as the first symptom. The first symptom in 95 per cent of these cases is pain. Since this patient had constipation for three or four days before he had pain, it is impossible for me to accept that diagnosis, and I cross a line through it.

What about an inflammatory process? That is the thing on which I have been trying to get Dr. Holmes to help me out. He has done the best he could. Did this old man have appendicitis?

DR. HOLMES: I might give more help by interpreting what is in the record. It says that the mucosa appeared to be intact. That would make one think the lesion was outside the bowel. Then it says that the lumen changed considerably in size.

DR. MCKITTRICK: All except one place.

DR. HOLMES: Yes, but that changed a little, as I read it.

DR. MCKITTRICK: Let us make sure of the quotation. "An area approximately 2.5 cm. in diameter at the beginning of the narrowed ileum never showed distention." I interpret that to mean there was a place 2.5 cm. long that stayed as it was.

DR. HOLMES: Perhaps that is a better way of interpreting it. At any rate I believe they were thinking of something outside the mucosa.

DR. MCKITTRICK: Of course this question of appendiceal abscess is of greatest importance. Could this man have such a lesion? One teaching that we have always been brought up to believe is that appendicitis in an old man is a queer dis-

ease and never gives the classic picture. It comes when we least expect it. I was hopeful that something in the x-ray report would indicate a pressure defect on the cecum to suggest that this man did have an appendiceal abscess. At the moment I shall put a question mark beside this diagnosis.

Next is the question of intrinsic inflammation. Could this man have had a process in the wall of the bowel itself that had left the mucosa intact? It seems to me that if he had had regional enteritis, tuberculosis or anything of that sort he would have had some symptoms prior to ten days before admission. I do not believe one is entirely safe in excluding such a process because the history is short, but it does seem that the history is too rapidly progressive for that type of lesion. I am unwilling to accept either regional enteritis or tuberculosis as the cause of this man's trouble, and I shall cross them out.

Then we come to the group of tumors. Did the patient have carcinoma, lymphoma or leiomyosarcoma? Again, the story is too acute and rapidly progressive for carcinoma of the terminal ileum, unless it had intussuscepted. If it had, the initial symptom, I think, would have been pain and not constipation. So you see, I can talk myself out of everything I can think of. We can possibly attach some significance to one statement of the X-ray Department, namely, that the mucosa in this area was intact. If the mucosa was intact, the lesion could not have been cancer. It probably was not lymphoma. So I cross a line through that group, and that brings me back to the question of an external inflammatory process.

Was this appendicitis? I cannot answer the question. I do know this—there is nothing in the story inconsistent with it. Appendicitis can result in secondary obstruction. I do not know how much attention to pay to the widespread rigidity and tenderness. I do not know whether the subnormal temperature means anything, but I do not believe it does. The white-cell count and differential mean nothing. The patient was eighty years old, and a person may have appendiceal abscess at that age. I shall have to say that he had small-bowel obstruction, that the lesion was probably extrinsic and that the likeliest extrinsic lesion is an inflammatory process, probably originating in the appendix.

DR. E. PARKER HAYDEN: I should like to ask Dr. Holmes if lymphoma can be excluded on the lack of destruction of the mucosa. I believe that a normal mucosa can be found with lymphoma.

DR. HOLMES: That is true, but an ulcerative lesion can also be present. If one is trying to decide between carcinoma and lymphoma, and

if the mucosa is intact, the lesion is a little likelier to be lymphoma. Perhaps Dr. Mallory can answer that better than I can.

DR. TRACY B. MALLORY: There is one other neoplasm in this area that should be considered more seriously than those two, that is, carcinoid. The mucosa is never ulcerated with a carcinoid, but I think the pattern might be altered.

DR. MCKITTRICK: Do they occur in the terminal ileum?

DR. MALLORY: Yes; next to the appendix that is the favored spot, and I have seen one in an eighty-year-old man.

CLINICAL DIAGNOSIS

Mucocele of appendix, with mechanical obstruction.

DR. MCKITTRICK'S DIAGNOSIS

Abscess of appendix, with secondary small-bowel obstruction.

ANATOMICAL DIAGNOSIS

Mucocele of appendix, with mechanical obstruction.

PATHOLOGICAL DISCUSSION

DR. NATHAN D. MUNRO: After the Miller-Abbott tube was in place, the general pain, tenderness and spasm subsided. The patient later developed an indefinite tenderness in the right lower quadrant. The x-ray films were of considerable help. The differential diagnosis was much as Dr. McKittrick suggested. Dr. D. N. Sweeny operated and found a mucocele of the appendix, which was reported to show subacute inflammation. It was adherent to the terminal ileum and was evidently the cause of the obstruction.

DR. MALLORY: Before it was opened the mucocele was sufficiently distended to make a small but significant tumor mass.

DR. MCKITTRICK: May I add that I got the greatest satisfaction out of reading this case over because of the way it was handled. Here was an eighty-year-old man with small-bowel obstruction and distention who undoubtedly would have died promptly after an emergency operation. The passage of a Miller-Abbott tube, with relief of distention, and later x-ray visualization of the obstructed area were just the things to have done.

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PROPAMIDINE—A NEW WOUND ANTISEPTIC

A RECENT issue of the *Lancet* focuses attention on a new antibacterial agent for topical application in infected wounds. In a study of the effect of the aromatic diamidine series on protozoa Fuller¹ noted that propamidine (4,4' diamidino diphenoxypropine dihydrochloride) also possessed an antibacterial effect. This substance has been carefully studied by Thrower and Valentine,² because its bacteriostatic action is not inhibited by peptones, tissue fluids, pus or para aminobenzoic acid. The lowest concentration of propamidine showing a clear bactericidal effect on hemolytic streptococci in pus was 0.003 to 0.005 per cent. For staphylococcal pus the effective concentration was 0.025 to

0.050 per cent. Studies of broth cultures suggested that the anaerobic gas producing bacilli were about as sensitive as staphylococci. In vitro phagocytic tests performed with defibrinated blood and staphylococci showed that phagocytosis was practically unaffected by 0.1 per cent propamidine, slightly reduced by 0.2 per cent and inhibited by 0.4 per cent. Even in a concentration of 0.4 per cent the leukocytes were not killed and the red cells were not hemolyzed. Thus it would appear that bactericidal concentrations of the drug are well below the cytotoxic level.

A clinical technique for the application of propamidine to wounds was evolved by trial on patients with osteomyelitis, infected burns and septic wounds of the soft parts. The wounds are cleansed with physiologic saline solution and are surgically exteriorized by incision, if necessary to ensure adequate contact of the drug with all infected surfaces. One tenth per cent propamidine in a base consisting of 45 per cent methyl cellulose in water is applied as a jelly to the wound surface and sealed over with vaseline gauze. The wound is dressed and similarly treated on alternate days for a total of five treatments. Care must be taken to avoid contact with the intact skin lest it become inflamed and irritated by the jelly. Treatment for more than ten days or concentrations above 0.1 per cent have led to superficial necrosis of the granulation tissue. It is apparent that the full antibacterial effect is readily obtained within the ten day period. Streptococci disappear first and are followed by staphylococci. Proteus and pyocyanus bacilli usually persist but do not appear to retard healing. Wounds with persistent sinuses or incomplete healing after the ten day period of treatment are judged ready for operative removal of foreign bodies, sequestrectomy or skin grafting.

Propamidine jelly was released for trial at an EMS hospital in 5 cases of infected ulcer and casualty wounds and 8 cases of burns.³ The infected ulcers and wounds became sterile, or nearly so, in four to ten days and thereafter healed rapidly or were successfully grafted. The burned patients were relieved of pain, second degree areas

healed within ten days, and infection did not occur. Morley and Bentley⁴ obtained similar results in 7 cases of recent burn and are of the opinion that propamidine was effective in the treatment of older burns infected with sulfonamide-resistant organisms.

McIndoe and Tilley⁵ used propamidine jelly in 11 patients with secondary hemolytic streptococcus infections of wounds and burns not improved by local applications of Eusol and sulfanilamide or by saline dressings. Recently infected wounds cleared more rapidly than older ones, but the streptococci disappeared from all within the ten-day period. In 3 cases there was partial loss of subsequent skin grafts from staphylococcal infection.

It is to be hoped that further trial of propamidine will confirm these encouraging reports. There can be little doubt that the drug will be exhaustively studied in the near future. No success has attended the intravenous use of propamidine in experimental streptococcal infections in mice.¹ Furthermore, clinicians will do well to note that drugs of this series have produced circulatory collapse or violent itching after the intravenous injection of 2 mg. per kilogram of body weight for sleeping sickness.⁶ It seems likely that absorption of topically applied propamidine will be slight, but this is an inference from the behavior of the related and fluorescent compound, stilbamidine,^{7, 8} which is stored in the liver and kidneys and is absorbed by the red blood cells. The possibility of immediate and late toxic effects is apparent. Until more experience has been gained it is unwarranted to use the drug for large wounds or in patients with impending shock.

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BOSTON'S AMPHIBIAN HOSPITAL

A SEA-GIRT country such as ours can boast of more than one floating hospital—of which the Navy's hospital ships are the present outstanding examples; only Boston can boast of an amphibian hospital that has breasted the unruly ocean for season after season, and finally climbed onto the land, not to rest but there to continue its labors. A unique Boston charity, the Boston Floating Hospital has now dropped the limitations imposed by the pure charitableness of its nature and has made its facilities available to those who can pay.

The Boston Floating Hospital was largely the product of the labors of the Reverend Rufus P. Tobey, who, with the aid of Edward Everett Hale, Dr. Francis P. Brown and others, chartered the barge *Clifford* in 1894. In the summer of that year the boat made five excursions down the harbor, bearing mothers and their ailing offspring for a day's outing. In the following year the *Clifford* was purchased and daily trips were made; and in 1896 the barge was transformed into a real hospital ship, with permanent wards, attending physicians and a training school for graduate nurses. In 1906 the *Boston Floating Hospital*, as a generation of pediatricians knew her, was built, and for twenty-one years continued her voyages of mercy with her cargoes of sick babies from the North End, the West End and the South End. There, also, important work was done in the study of infectious diarrhea and in the development of suitable foods for infants. The ship burned in 1927, and owing to less need for a hospital of this sort, largely because of the great decrease in the incidence of summer diarrhea, it was decided not to rebuild her. She had performed a great service.

Then the amphibian nature of her character was revealed, for out of her ashes, phoenixlike,—and after a dormant period passed in the vicinity of the Harvard Medical School,—came a metamorphosed and thoroughly landlubberly Boston Floating Hospital, entirely rid of the tang of the sea, primly and with the utmost stability associated with the Tufts College Medical School and the

Boston Dispensary to form the New England Medical Center. In 1931 the new ship, of stone and brick and concrete, was warped into place beside the remodeled Boston Dispensary, and there she lies, high and dry and thoroughly free of barnacles.

Dr Henry I Bowditch was for many years physician in-chief of the seagoing floating hospital, Dr Elmer W Barron presided over its terrestrial destinies until the fall of 1942, when Dr James M Baty took up the post by the binnacle. And now, at last, patients are to be allowed to help pay their own way, and they will not have to go aboard by a gangplank.

OBITUARY

ELLIOTT GRAY BRACKETT 1860-1942

To appraise adequately the loss of one who has for so many years served the public in so many ways and accomplished it so unobtrusively, unselfishly and untringly as did Elliott Gray Brackett, cannot be done by any one person. His character was a jewel of many facets and it mattered not from what angle it was viewed, nothing but serenity, understanding sympathy, and quiet, tireless devotion to the tasks that were before him were reflected from it.

His was a life of unstinted devotion of all his talent to the service of his patients. His records reveal how meticulous he was to note every material fact bearing on the conditions he was called on to treat. No detail was too trivial to attract his attention, and in his effort to arrive at a true estimate of the significance of reported symptoms he did not confine himself to physical signs. To an unusual degree he acquired an understanding of the bearing of seemingly wholly extraneous circumstances that often exerted a psychic influence over the purely physical complex. In his association with patients he so invariably convinced them of his complete absorption in their problems that they were impressed by the feeling that they were not merely "another case, to be dealt with in the routine way, but deserved the utmost of his skill to unravel their difficulties and provide the most appropriate treatment. To this initial care he added a 'follow up' that left no doubt in their minds that he was wholeheartedly concerned with their progress toward recovery.

No one who was privileged to work with him could fail to appreciate the value of this attitude

toward the practice of a profession. This would probably be particularly true of the specialty to which he devoted his life, where so much depends on attention to minutiae in dealing with conditions which are usually chronic and involve to an unusual degree the maintenance of a morale essential to success. And so it was that the organization of his office was such, over many years, that it reflected the spirit which motivated him and helped in the achievement of the goal for which he strove. It mattered not to him what the social statuses of his patients were, whether he met them in an outpatient clinic or they came to him as private patients, they commanded the complete absorption of his attention.

As an instance of this, during the last day of his life he had his mind so much on his patients' welfare that he had his shopman bring to his bedside a brace he had planned, in order that he might see that it had been made as he wished it to be.

Because he was a past master in the fitting of apparatus, he used braces and other means of support to a greater extent than many present day practitioners. He did excellent surgery when he thought surgery was indicated, but was never hurried into it before he had reason to think it would be the opportune time. I imagine it would be the consensus among those who worked with him as assistants over any considerable period that his judgment of the proper time to resort to operative surgery and his ability to control patients until that time arrived were, in the first respect, sound, and, in the latter respect, no less remarkable. His familiarity with the literature of his specialty and his acquaintance with its ablest exponents served to make him "not the first by whom the new is tried, nor yet the last to lay the old aside." In other words, though conservative, based on his experience, he was open minded to the last years of his activity.

To appreciate the esteem in which he was held by all who had been under his care, one should see the many letters that have come from his former patients. And it was not only from those whose association with him had been that of patient with physician, there are numberless letters from physicians who, at one time or another during their student years, had come under the spell of his influence. He had a way of impressing his personality on them which prompted many of them to feel that he had influenced their whole lives, inspiring them with his ideals and compelling them to make acknowledgment of their indebtedness to him.

He had unusual opportunities to make such contacts because of the many positions he occupied where younger men were brought into relation with him. A long service at the Children's Hospi-

tal in Boston, at the House of the Good Samaritan and the Boston City Hospital, followed by the headship of the Orthopedic Service at the Massachusetts General Hospital, and latterly at the Faulkner Hospital, brought him in contact with many undergraduate medical students, interns, residents and graduates taking refresher courses, from all over the country. In addition, his position since 1922 as editor of the *Journal of Bone and Joint Surgery*, the official organ of the American and the British orthopedic associations, made him acquainted, often quite intimately, with the leaders of thought and clinical activity the world over.

All these contacts, through clinical channels as well as by virtue of his journalistic work, served to keep him abreast of what was going on in the orthopedic world. The organization of the American Academy of Orthopaedic Surgeons and its affiliation with the *Journal of Bone and Joint Surgery* have added many new contributors to that journal and consequently have widened his acquaintance with several hundred younger men, now actively engaged in practice, who are the coming contributors to official orthopedic publications.

It was his custom for many years to take at least a two months' holiday in Europe, and while there he availed himself of the opportunity to attend meetings of orthopedic societies in various countries on the Continent and in the British Isles. It was at these gatherings that he succeeded in arousing interest for the journal in many foreign countries, where there are now a considerable number of subscribers, and even contributors.

His visits to Europe almost always found him centering his activities from Geneva, and it was there that he became an interested student of the questions that the League of Nations was attempting to solve. In fact, he took the necessary courses at Geneva to earn the League's diploma. He felt strongly that the future of the world's peace, as well as social and economic security, is dependent on some organization comparable to that for which the League was striving.

Honorary membership in many foreign orthopedic societies came to him as a result of his frequent attendance at their meetings and of his position as editor of the *Journal of Bone and Joint Surgery*.

Here in Boston his influence has been actively felt in such organizations as the School for Crippled Children and the Society for Occupational Therapy. He was a member of the Boston Orthopaedic Club and the Boston Surgical Society. The R.C.R.C. (Roxbury Clinical Record Club) had Dr. Brackett as one of its originators. He was a mem-

ber of the Massachusetts Medical Society, the American College of Surgeons and the Vermont State Medical Society. He served as chairman of the Professional Committee of the International Society for Crippled Children.

In the American Orthopaedic Association there was no one more universally respected. For several years he was treasurer of the society, and its president for one year; but beyond doubt his greatest service was rendered during the twenty years that he edited its journal, now the outstanding publication devoted to orthopedic surgery.

During World War I he was called to the Surgeon General's Office in Washington to head the orthopedic branch of the Expeditionary Force, selecting and allotting members of that specialty to service abroad or in this country. Later he was sent overseas, where he spent considerable time near the front, returning with the rank of colonel in May, 1920.

The Rockefeller Foundation, learning that Dr. Brackett was thinking of visiting China, invited him to give a course of lectures to the medical students at Peking Union Medical School and to demonstrate the methods of treatment employed in American clinics. At Shanghai and at Shantung Christian University were located two of his former house officers, with whom he spent some time.

These are without doubt not all the channels through which he quietly made his influence felt, for ostentation was foreign to his nature.

He showed few indications of any toll that advancing years and an almost lifelong handicap to his physical activities had imposed on him. I never heard him refer to this handicap.

Although in all the years I knew him he never gave expression to any conviction he may have had on religious matters, he stands out in my thought as the nearest approach to the ideal Christian gentleman—the exemplar of the Great Physician. The philosophy of his life would find some parallelism in the following quotation:

To live; to love; to die; to live again;
This is the all of being; but how large
Looms that adventure in the afterward!

Nor life, nor love may here survive, but there
Shall both endure, nor by endurance lose
Their zest. New opportunities for use,
New scenes, new joys, a sense of gratitude
For things mysterious made manifest
Shall there be mine, and not a thought intrude
Regretful of the past. My soul awaits
Expectant the transition. Do I hear
The plash of Charon's oars?

Ho! Ferryman

This way!

C. F. P.

MEDICAL EPONYM

TAWARA'S NODE

Dr. Sunao Tawara (b. 1873), working in the laboratory of L. Aschoff in Marburg, presented the results of his studies, covering a period of two and a half years, in a monograph entitled *Das Reizleitungssystem des Säugetierherzens. Eine anatomisch-histologische Studie über das Atrio-ventrikulärbündel und die Purkinjeschen Fäden* [The Conduction System of the Mammalian Heart: An anatomicohistologic study of the atrioventricular bundle and the Purkinje fibers] (Jena, 1906). The node is described on pages 183 and 184 as follows:

The system uniting auricle and ventricle forms a complicated muscular network of relatively large dimensions in the region just above the fibrocartilaginous atrioventricular septum, which we have termed a node. In one direction there courses from this node posteriorly a short bundle of fibers, arranged in a more or less parallel fashion, as far as the anterior portion of the coronary sinus, where it unites with the ordinary fibers of the auricle. In the other direction the node extends forward, growing rapidly smaller, to the ventricular portion and enters the ventricular septum after penetrating the fibrocartilaginous septum.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

BREECH DELIVERY: RESULTANT
INJURIES TO THE NERVOUS SYSTEM

Injuries may occur to the peripheral nervous system, the spinal cord, and the brain during breech delivery.

Two portions of the peripheral nervous system may be injured, the lumbosacral plexus and the brachial plexus. Rather rarely traction on the legs, while the infant's body is still firmly held in the mother's birth canal, can produce injury to the lumbosacral plexus, with flaccid paralysis of the legs and sphincters and subsequent atrophy of the thigh and gluteal muscles. Subluxation of one of the lower lumbar vertebrae has been occasionally demonstrated in such cases.

Traction on an arm or shoulder, with the head fixed in the mother's pelvis, may injure the brachial plexus. Tearing of the plexus from above downward usually occurs, so that the injury is likely to be severest in the nerve roots or trunks derived from the fifth and sixth cervical nerves, with the brunt of the paralysis in the muscles of the shoulder girdle. Generally the whole arm is temporarily paralyzed at birth, and the paralysis is maximal immediately after birth. Occasionally the whole

plexus is torn in such a delivery, and rarely the brunt of the injury involves the nerves of the hand. In a few such cases a history of an extended arm during delivery is obtained, and the inference is that the plexus was torn from below upward. Injuries involving the lower portion of the brachial plexus generally involve the cervical sympathetic trunk, often with the production of a complete Horner's syndrome.

Two modes of injury may affect the spinal cord. Owing to the fact that the infant's spine is more elastic than the contained spinal cord, traction on the infant's pelvis with the head fixed in the mother's pelvis results in stretching of the spinal column and rupture of the dura and spinal cord in the thoracic portion. This accident is reported to be accompanied by a loud snap. Flaccid paralysis and anesthesia below a given level, present immediately on delivery, are the usual signs. If a large enough segment of spinal cord is isolated below the injury, automatic sphincter and reflex phenomena in the legs soon develop. Incomplete rupture of the cord may be produced, with no complete anesthesia and with loss of motor power below the level of injury.

The spinal cord may also be injured by avulsion of the roots of the brachial plexus from the cord by traction on a shoulder or arm against a fixed head. The result is hemorrhage into the cord, with symmetrical flaccid paralysis of both arms, often more marked on one side, and with varying degrees of loss of sensation below the level of injury. If severe, such injuries are permanent. Minor injuries of this type accompany most brachial palsies and tend to clear spontaneously in a few weeks. There is some evidence to suggest that they may remain latent and in young adult life give rise to degenerative processes in the cervical spinal cord.

Injury to the brain during breech delivery results, at least in certain cases, from displacement of the cranial contents. Normally, the falx and tentorium act as supports for the brain, preventing its downward displacement into the foramen magnum. During breech delivery, traction on the already delivered trunk is transmitted to the spinal cord and puts the tentorium under strain. When suprapubic pressure on the undelivered head is added, the strain may be increased to the point where the tentorium ruptures. When this occurs the brain is displaced downward and the medulla herniates through the foramen, thus damaging the respiratory center. In addition, the vein of Galen is torn or angulated, and this interferes with the venous drainage from the basal region of the cerebrum. General fetal anoxemia results from the injury to the respiratory apparatus, and in

addition, especially severe injury may result to the region of the basal ganglia and other structures surrounding the third ventricle.

Finally, injury to the calvarium, with fracture or hemorrhage over the surface of the brain, may occur, usually as a result of suprapubic pressure or the application of forceps to the after-coming head. Such an injury may produce signs of intracranial distress, such as convulsions and asphyxia, at once, or if damage involves the cortex only, its effect may be apparent as hemiplegia, quadriplegia or mental defect as the baby develops.

The structure of the nervous system is well adapted to forces of compression exerted during labor, provided they are not continued over too long a period; but in general the nervous system cannot withstand the stresses and strains imposed by forces which tend to stretch the baby.

WAR ACTIVITIES

INDUSTRIAL MEDICINE

DERMATITIS INVESTIGATION IN SEATTLE SHIPYARDS

The chloracne among electricians in Seattle shipyards, which caused considerable alarm and a threatened strike, was due to the type of cable used and the fact that the electricians handled it continuously, reported Dr. Louis Schwartz, who made the investigation. Only one shipyard had cases of chloracne. The three remaining yards used another type of cable and electricians spent only part of their time stripping.

The alarm and the threatened strike in the Seattle shipyards followed newspaper reports of a dermatitis outbreak and 3 deaths due to acute yellow atrophy of the liver among workers at the Anaconda Copper Company, Hastings-on-the-Hudson, New York. The Seattle electricians were handling wire made by the Anaconda Copper Company and some of them had developed a dermatitis that they attributed to handling the wire. They were finally persuaded to remain at work until someone from the United States Public Health Service could arrive and make an investigation. Dr. Louis Schwartz immediately flew to Seattle where he examined workers who had the so-called "cable rash" to determine if it was a chloracne.

The cable which caused the acne was found to be the Anaconda cable in which asbestos impregnated with chlorinated compounds is loosely packed and flakes off during stripping operations. Precautions recommended by Dr. Schwartz for handling this special Anaconda cable with the loose insulation are as follows:

(1) Workers engaged in stripping cable containing either chlorinated naphthalene, chlorinated diphenyl or chlorinated diphenyl oxide should be supplied with hood respirators. It is preferable to have these hood respirators made from a transparent synthetic resin, such as plicofilm or vinylite, or perhaps from a fire-proof cellophane. The eyepiece should be a large flat plate of lucite rather than the conventional double lenses. The respirator should be closely fitted to the nose and contain such filters as will efficiently remove dust and wax.

(2) Workers should be supplied with clean overalls daily, the overalls to be laundered at the plant.

(3) Workers should wear long underclothes and change them daily.

(4) Workers should be required to take a shower before going home, and they should be furnished with toilet soap for this purpose.

If the hood respirator cannot be obtained or used, protective ointments of the type that coat the skin with a dry film and prevent the halowax from touching the skin should be applied to the face, neck and ears. Two such ointments are the tetryl protective cream developed by the United States Public Health Service, obtainable from the West Disinfectant Company, and a preparation Sav Skin No. 2, obtainable from the Doak Company, Cleveland, Ohio. These ointments should be applied before going to work, washed off before going to lunch, reapplied after lunch and washed off before going home.

At the end of the investigation, a meeting of the dermatologists in Seattle was called and 4 cases of chloracne were presented before them to acquaint them with the diagnosis and the recommended methods of treatment. — Reprinted from *Industrial Hygiene*, a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

MISCELLANY

PULMONARY TUBERCULOSIS RESULTING FROM EXTRAFAMILIAL CONTACTS

The possibility of the spread of tuberculosis within the family because of close contact cannot be too strongly stressed. The disease may attack as many as four generations. However, this should not obscure the importance of continuing the search for contacts outside the immediate household when case finding does not reveal the source of infection within the family. The importance of extrafamilial contacts is shown in a recent paper (Twinam, C. W., and Pope, A. S. Pulmonary tuberculosis resulting from extrafamilial contacts. *Am. J. Pub. Health* 32:1215-1218, 1942), from which the following is abstracted.

In mass surveys there is not the opportunity for individualization of cases that is necessary to discover extrafamilial sources of tuberculous infection. Rural communities with low death rates have afforded excellent opportunities for demonstrating the importance of extrafamilial contact in the spread of tuberculosis in the community.

In Massachusetts a five-year survey on the control of tuberculosis was recently conducted in a county considered to be representative of a rural New England community, and with next to the lowest death rate from pulmonary tuberculosis of any county in the state.

It was during this survey that attention was focused on the importance of extrafamilial contact. In March, 1935, and August, 1936, two cases of pulmonary tuberculosis were reported in a small community of approximately 4000 persons. Both cases were high-school girls, aged eighteen and sixteen respectively. They were the only young persons in their respective homes. Members of family A were examined and were found to have no evidence of tuberculosis. Family B refused examination at the time, but were subsequently examined and found to be negative for tuberculosis. There was no history of tuberculosis in either of the families. Both households used raw milk from tuberculin-tested herds, but obtained from different

duries The two girls were not chums but attended the same high school

A check with the school physician revealed that none of the teachers had tuberculosis, with the possible exception of one. She had suffered from pulmonary tuberculosis two years prior, but was discharged from the sanatorium as an arrested case. However, because several of the pupils complained that this teacher coughed during her classes, several sputum examinations were made by the school physician, all of which were found to be negative.

The situation rested at this stage until April, 1937 when a nineteen year old girl, graduated from the same high school in 1936, was found to have tuberculosis. Careful inquiry revealed that she had had little or no contact with either of the other girls at the school. She had, however, taken two courses given by the teacher who was under suspicion. An x-ray check up in her family showed no evidence of active tuberculosis, nor was there any family history of the disease.

Again the evidence pointed to someone in the high school as a potential source of infection for these three girls. The teacher, aware that she was under suspicion, returned to the sanatorium for a check up. A negative report was received by the school physician from the sanatorium.

In December, 1937, a fourth girl, aged seventeen, was found to have pulmonary tuberculosis. She, too, had had the same teacher in some of her classes. She knew all three of the girls but denied close friendship with them. Her family was examined roentgenographically by a local physician who reported negative findings. Subsequent examination of these films confirmed the original report. At this stage there seemed to be almost overwhelming evidence that these girls had had a common source of infection and the logical place to search seemed to be in the high school.

Further visits were made to the families to recheck their contact histories. They had all used raw milk from tuberculin tested herds, but only two of the families took milk from the same dairy. During one of these visits to family C a casual remark opened a new approach to the problem.

It was found that all four families attended the same church. This was a remarkable coincidence. A rough statistical calculation placed the church under strong suspicion on the basis that in the school population considerably less than half a case would be expected to have occurred by chance among this religious denomination if the source of infection were in the school. Inquiries regarding attendance of the girls at the church revealed that three of them sang in the choir and that all four of them had attended social functions on numerous occasions.

A careful check up of the reported cases and deaths in the community failed to show any of them to be members of this church. However, during the investigations relative to the church membership it was learned, quite by accident, that the wife of the former minister had developed pulmonary tuberculosis and had entered a sanatorium in another state within three months after leaving the parish, early in 1936. This rumor was checked and found to be authentic. In fact, at the time of admission to the sanatorium the minister's wife was found to have tuberculosis in an advanced stage and her sputum was positive.

Further inquiry revealed that the minister's wife also sang soprano in the choir and took communion from a

common cup before three of the girls who sang in the choir, as well as before the fourth who was not a choir member. Thus a common source of infection was found for these four girls in their fellow church member. On the basis of x-ray and sputum examinations and statistics, the schoolteacher, an arrested case, was eliminated from suspicion.

Aside from determining the true source of infection for these four girls, several other factors of epidemiologic significance are manifested. In this particular instance, the range of age was from sixteen to nineteen years and all cases were girls, again revealing the importance of age and sex. However, there is also evidence at the present time to show that the age of highest mortality from tuberculosis is gradually shifting to the older age groups.

A further factor of importance is that three of these girls had positive sputum at the time diagnosis was made. Two of them were moderately advanced and two far advanced at the time of diagnosis.

There was a high fatality rate. Two of the girls have died, one remains in a sanatorium and the fourth has been discharged from the sanatorium as an arrested case.

Although three of the girls sang in the soprano section of the choir, there was ample opportunity for contact between the fourth girl and the ministers' wife through social functions and Sunday school. These contacts were regular, usually once or twice a week over a period of several years.

The question of the common communion cup is a moot one. It is reasonable to suppose that droplet infection through contact at choir practice and social functions might well be sufficient to result in active disease. The dosage of infection was probably large if consideration is given to the cumulative effect resulting from frequent exposures at fairly regular intervals.

Failure to find the source of infection within a household should not preclude further attempts at finding the source. — Reprinted, in part, from *Tuberculous Abstracts* (March, 1943).

REPORT OF MEETING

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

A meeting of the Boston City Hospital House Officers' Association was held at the hospital on October 28, 1942. Dr. Edward I. Salisbury, associate director of the Medical Department of the United Fruit Company, spoke on the topic "Malaria."

This disease constitutes the greatest single medical problem of the armed forces in this war. It occurs in all regions in which troops of the United Nations are located, except Greenland and the British Isles. Even Australia has some endemic centers. Although Hawaii has not as yet reported any epidemic, this is almost certain to occur with the transportation of anopheline mosquitoes and their eggs. Mosquito control has been neglected in many regions of this country which are potentially endemic centers for malaria, and disastrous epidemics may result when returning members of the armed forces introduce a new strain of malaria. Anopheline mosquitoes are to be found throughout the extent of both the Atlantic and Pacific seaboard in this country, even to Alaska. There are also centers in the Midwest.

The disappearance of malaria from this country has largely been the result of a movement which has replaced wastelands and swamps with cities. But often ponds have been left for scenic or other reasons, and the fundamental factors for the initiation and spread of an epidemic of malaria are still present. These, then, may be activated by the return of our armed forces, either the wounded during the war or those returning after the war. Even New York and Connecticut have been known to have this disease, whereas Central Europe, especially Russia and the Balkans, are potentially endemic areas.

The prophylaxis employed by the armed forces against this scourge depends on the size of the group under consideration. If small, bed-netting, boots for the ankles and netting over the face when in the field may be used. When the group is large, the need of space for guns and other equipment makes the carrying of large amounts of such paraphernalia impracticable. For the proper carrying out of the recommended suggestions of the Army, each group should have an entomologist and a sanitary engineer.

The Army suggests that during the period when the engineers are improving conditions atabrine be given in doses of $1\frac{1}{2}$ gr. twice a day after meals two days a week, the doses being at least two days apart. Although it is recognized that no drug in safe dosage will prevent mosquito-borne malaria, this drug will suppress fever and decrease the symptoms. Signs and symptoms may develop on withdrawal of atabrine, and the Army advises the staggered withdrawal of the drug in large groups to prevent the mass appearance of malaria. Meanwhile, the entomologist and engineer should attempt to obtain proper conditions at the permanent site of a camp. Drainage of stagnant pools is not always the only thing to do, as evidenced by epidemics in India in which the vector is found only in running water. A capable entomologist will save a great deal of time by tracking down the vector quickly. Different *Anopheles* have widely divergent habits, some preferring sunny, open streams to the characteristic cool, shady pools.

The treatment of malaria started in the middle of the seventeenth century with the use of the crude bark of the cinchona tree. This was employed until 1820, when the alkaloid quinine was introduced. Quinine has been the drug of choice until quite recently, when several substitutes have been made available.

In 1926, plasmochin, the quiniline derivative of quinine, but obtained from methylene blue, was introduced and was found to be efficacious against *Plasmodium vivax* and the adult form of *P. falciparum*. But it was ineffective in combating the sporulating forms, which cause the clinical manifestations. It is good in combination with quinine, since both the adult forms and the spores are killed.

In 1932 atabrine was developed from a yellow dye. This is effective against the sporulating forms. It is a good substitute for but not equal to quinine. It was formerly employed in relapses, failures to quinine and idiosyncrasies. It is especially good in malaria during pregnancy and in blackwater fever, which seems to be precipitated by quinine. Some authorities decry the use of atabrine with plasmochin, but Dr. Salisbury and many others have used it without mishap for some years. A good seven-day intensive treatment is as follows: 10 gr. of quinine three times a day for three days and $1\frac{1}{2}$ gr. of atabrine for four days; and $\frac{1}{6}$ gr. of plasmochin is given three times a day for the last five days.

BOOK REVIEW

Ornithologists of the United States Army Medical Corps: Thirty-six biographies. By Colonel Edgar Erskine Hume, M.C., U.S.A. With foreword by Alexander Wetmore. 4°, cloth, 583 pp., with 109 illustrations. Baltimore: The Johns Hopkins Press, 1942. \$5.00.

This volume concerning Army surgeons who were also ornithologists will delight bird lovers and medical historians. In fact it will be a pleasure for all those who are interested in science to read of the remarkable accomplishments of this group. The numerous illustrations—photographs of the ornithologists, some of their drawings of birds and photographs of western Army posts—add much to the interest of the book. It is impossible to mention all the men whose biographies are given in this work. Some of the longer accounts of interest are those of Bendire, Cooper, Elliot, Coues, Mearns, Schufeldt, Casey Wood, Xantus and Yarrow.

Elliott Coues had much to say concerning his friendship with Bendire who confided to him his many trials and tribulations concerning misunderstandings with other ornithologists, particularly Dr. Brewer, and Dr. Coues was able to smooth out many of the troubles and misunderstandings. This resulted in the acquisition by the Smithsonian Institution of Dr. Bendire's large and valuable collection of eggs. In the biography of Coues, due mention is made of his greatest ornithologic works, *Key to North American Birds*, *Birds of the Colorado Valley* and *Birds of the Northwest*. Also, five of his original drawings are reproduced from the *Key*. Dr. Coues also made numerous expeditions for various government surveys. One of his most important works along this line was the account of the Lewis and Clark expedition. He wrote no less than fifteen volumes on his explorations. The biography ends with a touching account of Coues's later life by his great friend Daniel Giraud Elliot.

Edgar Alexander Mearns is one of the most fascinating figures pictured in these biographies. His medical and ornithologic experiences in the Philippine Islands are of extreme interest, as well as his exploration with the Frick Expedition to Africa, when, in less than ten months' time, Dr. Mearns collected fifty-two hundred bird skins. He was a victim of diabetes, unfortunately before the time of insulin, and was in poor health for many years. His energy and enthusiasm under the circumstances were remarkable. Dr. Mearns described and named a large number of birds.

The monumental work of Casey Wood on avian ophthalmology is given due praise in the biography of this famous physician. The exact title of this work was *The Fundus Oculi of Birds, Especially as Viewed by the Ophthalmoscope*. Dr. Wood was a medical historian of note, and the following interesting statement is made in his biography: "Col. Wood's last work or publication is a translation of the famous *De Arte Venandi cum Avibus*, written in barbaric Latin, a work on medieval ornithology and falconry by the Emperor Frederick II of Hohenstaufen (1194-1250 A.D.)."

Perhaps no work published of late has shown more adequately the selfless interest and devotion to science of such men as these. In the stress and strain of the present time, the book comes to those who are interested in ornithology, medical history and medical science like a fresh summer breeze over a salt marsh. The reviewer believes that it is the most valuable book of its type that has ever been published, and that it will undoubtedly bring great pleasure to its many readers.

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COMPOUND FRACTURES OF THE SKULL

A Study of 104 Consecutive Patients

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Je le pansay, Dieu le guarit

[I dressed the wound, God healed it]

REPEATED again and again in his writings, and making a memorial more lasting than the monument on which it is written, this phrase sums up Ambroise Paré's surgical beliefs.¹ Courage, humility and common sense changed this rustic barber's apprentice into the greatest surgeon of the sixteenth century. Long experience in wars as brutal and careless of human life as that now in progress taught him the value of letting well enough alone, and gave him his faith in the healing power of Nature. In his *Journeys in Diverse Places*, he² gives the following account:

All the seigneurs within the town asked me to give special care, above all the rest, to M de Pienne, who had been wounded, while on the breach, by a stone shot from a cannon, on the temple, with fracture and depression of the bone. They told me that so soon as he received the blow, he fell to the ground as dead, and cast forth blood by the mouth, nose and ears, with great vomiting, and was fourteen days without being able to speak or reason, also he had tremors of a spasmodic nature, and all his face was swelled and livid. He was trepanned at the side of the temporal muscle, over the frontal bone. I dressed him, with other surgeons, and God healed him, and to-day he is still living, thank God.

The passing of almost four hundred years has not changed the basic truth of the lessons learned and taught by Paré. New ways of "dressing the wound" have been found, but in no field of surgery is it more important to realize the need for avoiding irritation and for withholding middle-some procedures than in the care of patients suffering from compound fractures of the skull.

The observations to follow are based on a study of 104 patients admitted to the Rhode Island Hospital between January, 1940, and July, 1942. The

series includes, without further selection, all patients on whom a reasonable diagnosis of compound fracture of the skull was made. Ninety-eight of the diagnoses were made clinically, 6 were made by x-ray alone. Of the clinical diagnoses, 62 were confirmed by x-ray examination. It should be realized that an x-ray finding of fracture is not essential in making the diagnosis. The roentgen ray examination is a most valuable aid, and should be used whenever possible, but one should take care not to be misled by lack of evidence of this sort. Many of the more seriously injured patients in this series were never in condition to warrant the use of x-rays; in several, fractures were found at operation that did not appear in the films, and definite clinical findings of compound fracture were not infrequently unconfirmed by careful x-ray examination. Insistence on x-ray evidence before accepting a diagnosis of compound fracture of the skull may result in real harm to the patient through improper treatment.

Although these patients have been selected for study on the basis of their having a special type of damage to the skull, one should not lose sight of the fact that they had an injury to the head, and that here, as in all patients with head injury, the degree and extent of the brain damage were of the greatest importance in treatment and prognosis. A compound fracture should be regarded as a major complication in a patient suffering from damage to the brain. By the classification adopted in a paper³ read two years ago, 2 per cent of these 104 patients had concussion, 24 per cent had congestion, and 74 per cent had evidence of contusion, while 2 patients had no signs of brain damage. Comparing these figures with those for head injuries as a whole, 4 per cent of which had concussion, 47 per cent congestion, and 49 per cent contusion, the degree of brain damage, in general, is seen to be considerably severer in this group than in patients without this complication.

*Prepared for presentation at the canceled 1942 annual meeting of the New England Surgical Society.

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The small number of patients included in this study makes generalizations concerning age incidence of doubtful value. It may be of interest to note, however, that the ages ranged from one to eighty-three years, the most dangerous decades being from one to ten and from thirty-one to forty years. Forty-two per cent of the patients were injured in traffic accidents, 36 per cent in falls, and 19 per cent were struck in the head; 2 patients were hurt in airplane accidents, and 1 was wounded by a gunshot. Only 16 patients were injured in industrial accidents, in spite of the fact that the Rhode Island Hospital is located in a busy manufacturing center. Ninety per cent of all the injuries occurred in males.

A fracture is ordinarily held to be compound when, along with the break in the bone, there is a break in the overlying skin or mucous membrane such that infectious organisms are given a means of access to the fracture. When this commonly accepted definition is applied to fractures of the skull, compound fractures in this region fall naturally into three main groups—those of the base, of the paranasal sinuses and of the vault. Any classification of these fractures, unless so elaborate that it proves cumbersome, involves some overlapping and inaccuracy: several of the bones making up the base also help to form the vault, and lines of fracture may extend from one part to the other; fractures involving the sinuses not infrequently extend into the base; and multiple injuries add new difficulties. But this method divides these fractures into three definite clinical types, and is at least simple and workable.

Compound fractures of the base may affect the frontal, ethmoid, sphenoid, temporal or occipital bones; we have seen injuries in all these areas, but by far the greatest number are found to involve the petromastoid part of the temporal bone. Sixty-six of our patients had basal fractures, and 49 of these had damage in the petromastoid region. The diagnosis of compound basal fracture was made on the evidence of bleeding from the ear not otherwise explained, blood in the middle ear behind an intact drum, drainage of cerebrospinal fluid from the ear, bleeding into the pharynx not otherwise explained, x-ray films, or any combination of these. Bleeding from the nose was considered an unreliable indication, since the nasal bones are often broken without any fracture of the true skull. Nasal bleeding, however, should make one suspicious of skull damage. Patients with drainage of cerebrospinal fluid from the nose may have basal fracture or fracture involving the air sinuses; for the purposes of this study, they have been placed in the sinus group. X-ray confirmation of the diagnosis was obtained in 34 patients.

Basal skull fractures have, in general, a high mortality and a low probability of the patient's resuming a normal and useful life. When compounding, with the attendant risk of infection, is added, the outlook is considered even graver. But the condition of patients with compound basal fractures is by no means hopeless, and they will repay careful treatment. The treatment is primarily that of the associated brain damage. Many of these patients are in shock on admission, whereas others develop delayed shock. The blood pressure often holds up surprisingly well in patients whose vital functions are evidently depressed, only to fall suddenly when severe shock develops. We have come to consider the temperature as the most reliable indication of impending shock; any patient whose temperature is below normal is thought to be probably on the verge of shock. When shock exists or threatens, it must be treated before anything else. The patient is put to bed as quickly as possible; heaters and blankets are used to combat the fall in temperature; unless its presence interferes with necessary procedures the clothing is not removed, and then only under blankets without exposure; black coffee is given by rectum and caffeine with sodium benzoate under the skin. All unnecessary handling is avoided. X-ray examination is not attempted, and physical examination is strictly limited and is done without exposure. If there are fractures of the extremities they are fixed as simply as possible, with no attempt at correction. It is sometimes hard to convince the hospital staff of the importance of these measures, but their observance may mean the difference between life and death. Fluids are best replaced by the use of plasma; we are fortunate in having access to a supply of this substance. There is some evidence that the crystalline solutions used by vein in shock may increase the already heightened permeability of the smaller vessels and thus do harm.⁴ If plasma is not available, therefore, or if hemorrhage is a real factor, it is wise to use transfusions of whole blood.

When the shock has been remedied the brain and skull damage can be treated. If the breathing is poor or the oxygen exchange is hampered, oxygen is given, preferably by the use of a Burgess⁵ box. If the patient is excited, we omit the use of caffeine and give luminal sodium in the muscle. We do not use morphine, as we believe that this depresses respiration and raises intracranial pressure. When there is drainage of blood or cerebrospinal fluid from the ear, we use dry wipes to the auricle only; no attempt at cleaning out the canal or even examination is allowed until late in the course of treatment. The pharynx is kept clear of blood and mucus, when necessary, by position and

suction. If there is bleeding from the nose, we follow the same hands-off policy as in the case of the ear, hoping by these measures to avoid introducing infection. Lumbar puncture is not done on these patients until at least ten days after all discharge has stopped, as we believe that an outward flow is to be encouraged and that a possible reversal of flow by lowering the intracranial pressure may increase the chance of meningitis. For the same reason, we do not use dehydration. On the contrary, it is our belief that these patients need at least 2500 cc. of fluid, 5 gm. of sodium chloride, a proper supply of vitamins and 1500 calories daily. These are given by mouth when possible. If the patient is unconscious or unable to take liquids by mouth, they are given by the vein or by nasal stomach tube. We are convinced that many patients in this condition have, in the past, died of starvation and lack of fluids, and that giving proper amounts of liquid and nourishment will often keep the patient alive and allow Nature to "heal the wound."

Patients with fractures in the petromastoid region should be watched closely for the onset of infection. When a patient with such a fracture developed fever, it was formerly our practice to drain the mastoid process by operation, even though x-ray films showed no breakdown of the cells. With the advent of the sulfonamides, this procedure has become largely unnecessary, but we still follow it when the fever does not respond to treatment with the drug. Of the 66 patients in this series treated by these methods, 25 died, a mortality of 38 per cent. Twenty-one of these deaths occurred in the first twenty-four hours, many of them within an hour or two, so that there was little chance for any form of care to take effect. In the 45 patients who lived more than a day, 4 deaths occurred later, a mortality of 9 per cent. Two of these deaths were due to associated brain damage, and came on the third and fourth days respectively; 1 resulted on the twelfth day from a complicating subdural hematoma that was not recognized during life; and 1 came on the tenth day in a patient with acute mastoiditis, perisinus abscess and meningitis following fracture of the left mastoid process.

Compound fractures involving the paranasal sinuses may affect any of the air sinuses. Although it is likely that some of our patients classified as having compound fractures of the base had fractures entering into the ethmoid and sphenoid sinuses, we have not been able to recognize them definitely, either clinically⁶ or by x-ray examination. From the standpoint of treatment, however, this is not of serious importance, since recognized fracture extending into either of these sinuses

should be handled by the methods already outlined for fractures of the base. Twenty-one of the patients included in this study had fractures involving the air sinuses; in 10 patients, the maxillary antrum was affected, and in 11, the frontal sinus.

Wounds penetrating through the face into the antrum are, in our experience, rare; none were included in this series. When we have met such wounds, we have treated them by thorough débridement and cleansing, followed by a tight layer closure of the external wound, with drainage into the nose when needed. All the antral fractures in this study were of the closed type, and the diagnosis was made almost entirely on the basis of x-ray examination. The general treatment is that of the associated brain damage; locally, we have left these fractures alone, watching the patients carefully for the development of infection. In these 10 patients, there was no infection and no death resulted. There is always a considerable probability that fractures in this region may extend into the nearby basal areas; because of this, we withhold lumbar puncture for the same ten day period that we observe in known fractures of the base.

Compound frontal-sinus injuries fall into three main groups: closed fractures, where the compounding is into the sinus itself, without an overlying scalp wound; open fractures, with an external wound extending down to the fracture, and penetrating injuries, where the scalp wound communicates directly with the cavity of the sinus. The closed fractures are treated in the same way as are basal and closed antral fractures. Open fractures are transformed into closed injuries by débridement, careful mechanical cleansing and layer suture without drainage, and are then treated as closed fractures. The most serious injuries in this region are those with penetration of the sinus cavity; these patients often have dural tears, contamination or gross damage of the frontal lobe, and injury of the orbit and its contents. It is our belief that here, as in other fields of surgery, the least extensive procedure that will serve the purpose is probably the best one to follow. As a result, we do not routinely remove the posterior wall of the sinus⁷ or the entire lining mucous membrane,⁸ nor do we drain any area from which damaged brain tissue has been removed.⁷ Operation is done as early as possible. The external wound is débrided by the block excision of a hollow cone of damaged tissue about 0.6 cm. thick extending from the skin down to the bone, and any superficial loose bone fragments are removed. The instruments and gloves used in this dissection are then discarded, and the wound is flushed thoroughly with large amounts of sterile physiologic saline solution. In-driven

bone fragments or pieces that have evidently lost their blood supply are then removed; the one exception to this rule is in the case of the supraorbital ridge, which we have replaced on several occasions. Damaged brain tissue is removed by careful suction and an attempt is made to close the dura. This is often impossible because of tissue loss; when this condition exists, we wall off the part of the wound communicating with the brain by careful suture and close it without drainage. We have not used any foreign substance for dural closure,⁹ as we have feared that any such material might encourage the development of infection. When the damage to the mucous membrane is not too great, we close it, after making sure that there is good drainage through the nasofrontal duct. If the mucous membrane cannot be closed, we remove the injured edges and make a layer closure of the wound over it around a small rubber-tissue drain. It has been said that external drainage must be avoided at all costs, as it will inevitably result in the formation of a fistula.¹⁰ We have followed this method in 5 patients, removing the drain in a few days, when the danger of infection seemed to have passed; in each patient the wound healed well without further drainage. Eleven patients had compound fractures involving the frontal sinus; there were no deaths, and infection occurred in only 1 patient.

Drainage of spinal fluid through the nose is not infrequent in head injuries and may prove to be a serious complication; it always indicates a compound fracture, either of the base or of the air sinuses, and requires careful treatment. We have found conservative treatment to give good results. This consists of care of the general condition as already described and avoidance of any manipulation within the nose. Here again, we believe that the maintenance of an outward flow of fluid is important in avoiding infection; we do not use dehydration, and we delay lumbar puncture until ten days after all discharge has stopped. Five of our patients had definite leakage of cerebrospinal fluid from the nose; 1 died from severe brain damage within two hours; in all the others the drainage stopped in three to twelve days without the onset of infection. If a chronic draining fistula develops, it may be necessary to close the dural tear by one of the recognized methods. Up to the present time, we have not had occasion to do this.

Compound fractures of the vault divide themselves into three main groups: those without depression of the fractured bone; those with depression of the broken bone but without damage to the underlying dura; and those with injury of the dura and brain. In all of them, our basic aim is

to change them into simple fractures of the skull, and then to treat the brain damage.

If the patient has a compound fracture without depression, we débride the wound by the method already discussed under fractures of the frontal sinus. If dirt has been ground into the surface of the skull, we try to remove it by thorough washing with saline solution or by swabbing with gauze; when this is not enough we use a curet or burr until we reach clean bone. Linear fractures are left alone unless hair or other foreign matter has been caught between the edges; in such patients, the contaminated edges are removed. The wound is then closed without drainage by a carefully made layer suture.

When there is depression of the skull without damage to the dura, the depression should be raised. In children it is often possible to make a burr hole alongside the depression, introduce an elevator through this hole, and snap the depressed fragments back into position. In adults this can rarely be done; it is usually necessary to remove the fragments piecemeal. In any event, free bone fragments or pieces that have lost their blood supply are taken out so that they may not act as foreign bodies. Any resulting bone defect can be repaired later if this proves to be needed. The uninjured dura is left alone unless there is evidence of blood under it, or unless there are neurologic signs making exploration advisable.

When, in addition to bone damage, there is injury to the dura and brain, we follow the methods developed by Cushing¹¹ as a result of his experience in World War I. The basic principle is the early removal of all foreign matter and all devitalized tissue. The wound is carefully débrided, saline washing is used freely, loose bone fragments are removed, and the damaged dural edges are trimmed off. Brain tissue that has been injured beyond recovery is removed by suction. If pieces of bone have been driven into the substance of the brain, they are sought for with a small rubber catheter; gentle irrigation and suction through the catheter will often dislodge them, and if this is not successful they can be removed with fine forceps. Exploration with the finger for such fragments is unwise. Damaged brain tissue along the track made by the bone is removed through the catheter in the same way. Our experience with penetrating wounds made by bullets or other missiles has been limited, as our patients were not suffering from war injuries; such wounds are treated, in general, in the same way as those caused by bone fragments. Horrax¹² has recently suggested an interesting modification of Cushing's method—the excision of the wound track by electrocoagula-

tion and strong suction. To date we have not had an opportunity to use this method. After the foreign bodies and damaged brain tissue have been removed, the dura is closed as well as possible, and the external wound is closed by careful suture in layers without drainage.

Seventeen patients had compound fractures of the vault. There were 4 deaths in this group, all from associated brain damage. No patient became infected.

The likelihood of infection in compound fractures is the chief difference between them and simple fractures. On the basis of our experience up to the present time, we believe that infection in compound fractures of the skull can be largely avoided by the following methods:

Minimal handling of the wound

When there is an external wound, we explore it gently with a sterile gloved finger to determine the presence of fracture. We then cover it with dry sterile gauze and do not try to clean it or its surroundings until we operate. When the wound involves the ear, nose or pharynx, we do not investigate or clean these cavities; we simply try to see that drainage from them is not blocked by any dressing.

Avoidance of reversal of drainage

We do not use lumbar puncture or dehydration until ten days after all bleeding or drainage of cerebrospinal fluid has stopped. In patients with compounding as shown by x-ray study but without external bleeding or drainage, we observe the same precautions until ten days after the injury.

Early operation

Our aim is to operate on patients needing such treatment within six hours of the time of injury. By using the methods already described the shocked patient can usually be made operable within this period. When the patient's condition is doubtful, we use transfusions of plasma or whole blood throughout the operation, with good results.

Thorough débridement and mechanical cleansing

We try to remove all foreign bodies and all contaminated or devitalized tissue by excision, curetting, washing with sterile saline solution and suction.

Avoidance of surgical drainage

All wounds, except those of the frontal sinus, are closed by careful suture in layers without drainage.

The advent of the sulfonamides has not lessened the basic importance of these methods. In injuries of this character, drugs will not take the place of careful surgery. They are useful in checking beginning infections or in treating established ones, but it is our belief that they should be used in the blood stream and given either by mouth or intravenously. There is evidence that they may be definitely irritating when they are used directly in the open wound.¹⁸ If, for any reason, operation is delayed for over six hours, we sometimes dust the wound lightly with sulfanilamide powder, hoping thus to delay bacterial activity. At the time of operation, however, the chemical is removed along with other foreign bodies, and none of it is knowingly left in the wound.

In this series there was no wound infection. Two patients developed meningitis.¹⁴ One of them, already mentioned, had a basal fracture through the mastoid process followed by acute mastoiditis, perisinus abscess and death from meningitis due to an unidentified organism. The other had an open fracture of the frontal sinus followed by pneumococcal meningitis, which cleared up with the use of sulfadiazine and antipneumococcus serum, the patient making a good recovery.

Operative treatment was used in 28 patients. Ten patients had débridement and suture and all recovered; 13 had débridement, elevation or removal of depressed or in driven bone fragments and suture, and all of these recovered; 2 patients had complicating extradural bleeding and 1 of them died; 1 had a complicating subdural hematoma and died; 2 had exploration of the mastoid process, and both died. The operative incidence was thus 27 per cent, and the operative mortality was 14 per cent.

SUMMARY

A study of 104 consecutive patients with compound fracture of the skull is presented.

As the main injury, 66 had fractures of the base, 21 had involvement of the paranasal sinuses, and 17 had injuries of the vault.

There was no wound infection, and 2 patients developed meningitis.

The operative incidence was 27 per cent, and the operative mortality 14 per cent. The overall mortality for the entire series was 28 per cent.

These patients were treated by methods aimed at guarding and helping the natural healing processes of the body.

Je le pansay, Dieu le guarit

184 Waterman Street

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A YARDSTICK FOR RHEUMATOID ARTHRITIS*

Applied to Patients Receiving Gold-Salt Therapy

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"CHRONIC arthritis" is a term that has covered a multitude of joint conditions, and only fairly recently has a definite and intelligent division of the chronic arthritides been brought into being. However, to our mind the understanding of the various phases and of the as yet unpredictable course of rheumatoid arthritis leaves much to be desired, even in the minds of those most intimately associated with and well informed about the disease.

An analysis of fifty-four medical papers dealing with rheumatoid arthritis in seven leading medical journals for the years 1936 to 1940, inclusive, reveals that only one paper fails to separate in its discussion the two main arthritic groups of patients, that is, those with degenerative joint disease (hypertrophic arthritis or osteoarthritis) and rheumatoid (atrophic) arthritis. However, the division of rheumatoid arthritis into its active and inactive stages, admittedly difficult, was much less well handled. Forty-three of the fifty-four author-groups recognized the existence of these two stages of the disease, but only nine of the fifty-four attempted to analyze their case studies or therapeutic results, bearing in mind the difference between the active and inactive stages of the disease. This, it seems to us, is at once an understandable and yet deplorable condition. Certainly the study and treatment of chronic inactive rheumatic heart disease and the active rheumatic fever state are never considered simultaneously, yet the comparison of these two conditions with inactive and active rheumatoid arthritis does not seem farfetched. Realizing the inherent difficulties in such a division of these states, but believing that an attempt should be made to clarify the situation, we are presenting a

simple objective numerical formula that is, in our experience, useful in separating the active and inactive stages of rheumatoid arthritis, and can be used as a therapeutic yardstick in the treatment of both the active and inactive stages of the disease. The application of this yardstick of therapy to the treatment of active rheumatoid arthritis with gold salts is presented here. The six more reliable commonly used objective clinical and laboratory observations in rheumatoid arthritis have been combined into what we have termed the "ADDICT chart" (Fig. 1). These are, in order of use, as follows:

A. Functional Activity. This has to do with the physical ability of the patient in its entirety. It is, in addition, a measure of whether the patient is or is not dependent on his family or the community. The subdivisions (0 through 4) are self-explanatory, and indicate physical as well as socioeconomic levels at which the patient exists at the time of the examination.

D. Disease Activity. This deals with the objective measurement of inflammatory changes that present themselves to the clinical observer at the time the patient is seen. The same range of subdivision as for functional activity has arbitrarily been set up, and the classic clinical signs of increasing joint inflammation used. For the measurement of changes subsequent to treatment or the status of the inflammation at any one time, it seemed wisest to use the patient's most active or inflamed joint as the one to be recorded. Varying degrees of activity are found in a number of different joints in the same patient, and joints that on pathological examination have appeared clinically inactive for years may show an active inflammatory process when examined microscopically. These facts make the use of D_1 of less practical value as an isolated observation, but if the simple criteria outlined in the chart are used and the relation of this measurement to the whole disease process is carefully reviewed, we believe that this figure is a useful approximation of disease activity.

D_2 . Deformity. Deformity of a mechanical or static nature dependent on previous joint damage is recorded by the subdivisions. When subdivisions 1 and 2 are used,

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the examiner must be careful to ascertain that the periarticular thickening, painless swelling and crepitus or limitation of motion, or both, are due to static deformity, not to inflammatory changes about the joint. It is obvious that this objective observation in our formula is almost entirely a measure of mechanical deformity. The ortho-

I. Sedimentation Index This index, as well as other methods that measure the speed of erythrocytic sedimentation under standardized conditions, has long been recognized and proved to be a rough proportional measure of inflammatory activity in rheumatoid arthritis. We recognize that this is a rough laboratory measurement of

FIGURE 1 *Chart for Coding Status of Arthritic Patients*

CLASSIFICATION (F RATING)	REMARKS												
A—Activity of physical nature													
0 = Employable 1 = Ambulatory (able to get about alone) 2 = Confined to one floor bed and chair without assistance 3 = Confined to bed, needing part time assistance (able to feed and so forth) 4 = Confined to bed, needing full time assistance (helps)	For hospitalized patients this rating is made on probable functional ability if the patient was discharged on the day of examination. For example if the patient is confined to bed because of an operation the rating is either 3 or 4 depending on how sick the patient is.												
D₁—Disease activity *													
0 = None 1 = Tenderness or pain on motion or both 2 = Pain, tenderness and swelling 3 = Pain, tenderness, swelling and warmth 4 = A joint showing the maximum of active symptoms (heat and redness added to the other signs)	The rating should be made on the worst joint. Care must be taken in deciding whether signs are due to disease activity or to the results of the disease. Tenderness is elicited by pressure of the fingers without squeezing or moving the bones. Swelling must be distinguished from fibrous thickening or painless effusion. Warmth must be natural and not due to treatment.												
D₂—Deformity of static nature													
0 = None 1 = Periarticular thickening, painless fluid or crepitus on motion 2 = Limitation of motion 3 = Subluxation 4 = Ankylosis or flail joint	The rating should be made on the worst joint. Care must be taken to distinguish between real deformity and that due to disease activity such as pain which may in itself cause limitation of motion. If the disease is considered active these ratings can be made from a history of pre-existing painless periarticular thickening or limitation of motion. 3 and 4 can be determined even if the disease is active and should be recorded if they exist.												
I—Index of erythrocyte sedimentation													
0 = 0.5 or less 1 = 0.6-1.0 2 = 1.1-1.5 3 = 1.6-2.0 4 = 2.1 or more													
C—Color of hemoglobin													
<table border="1"> <thead> <tr> <th>Males</th> <th>Females</th> </tr> </thead> <tbody> <tr> <td>0 = 90-100</td> <td>80-90</td> </tr> <tr> <td>1 = 80-89</td> <td>70-79</td> </tr> <tr> <td>2 = 70-79</td> <td>60-69</td> </tr> <tr> <td>3 = 60-59</td> <td>50-59</td> </tr> <tr> <td>4 = 59 or less</td> <td>49 or less</td> </tr> </tbody> </table>	Males	Females	0 = 90-100	80-90	1 = 80-89	70-79	2 = 70-79	60-69	3 = 60-59	50-59	4 = 59 or less	49 or less	
Males	Females												
0 = 90-100	80-90												
1 = 80-89	70-79												
2 = 70-79	60-69												
3 = 60-59	50-59												
4 = 59 or less	49 or less												
T—Tissue turgor (body weight)													
0 = Normal or increased 1 = Loss 9 lb or less 2 = Loss from 10 to 19 lb 3 = Loss from 20 to 29 lb 4 = Loss 30 lb or more	The normal weight should be that which was average for the patient before the disease began, not the normal for age and height.												

pedic treatment of inactive rheumatoid arthritis joint disease by surgery or with apparatus produces the largest change in this objective division of the chart. The worst joint is used in measuring improvement in this division. Since involvement of the upper or lower extremity may affect A (Functional Activity) to an unusual extent, it may be necessary in certain cases under 'Remarks' to enlarge on the location of the worst joint and its importance to the patient, for example, ankylosis of the finger joint and that of a hip joint are quite different situations. However, in dealing with rheumatoid arthritis this is not so serious a difficulty as one might expect, because usually two or more joints of all those involved are at about the same stage of mechanical deformity.

a nonspecific physical state of the erythrocytes in the blood milieu. It errs grossly in certain individual cases, but on the whole is useful. Our subdivisions are arbitrary, but in our experience proportional to the activity of the disease. Change of the rate of erythrocytic sedimentation to a higher or lower level has been more useful than its absolute measurement in rheumatoid arthritis, a condition in which it is always eventually elevated.

C Hemoglobin Color The hemoglobin color or content of the blood is a moderately reliable laboratory measurement of rheumatoid arthritis activity in a large majority of patients. The presence of a hypochromic anemia that does not respond to iron therapy is frequent among patients with active rheumatoid arthritis, and its improve-

ment is of common occurrence in patients who become spontaneously better or respond to gold-salt therapy, as will be seen later on. The absence of anemia or a response of the abnormal condition to iron therapy usually indicates low-grade or early rheumatoid arthritic activity. The sex difference in normal values is used in making the subdivisions.

T. Weight (Tissue). Body-weight or tissue change is the last objective observation in the formula, and as is true of all three of the absolute measurements, a change in the degree of abnormality is of more value than the single measurement. For the purpose of recording, the normal weight is the average weight during the years in the patient's life that she or he had good health. In children, the average weight for chronological age and height is used. As will be shown, a real change for the better in the first five measurements of this formula is practically always accompanied by a change in the same direction in this measurement. Rheumatoid arthritis in its active stage has been found to be associated with weight loss of some extent.

ILLUSTRATIVE CASES

As the question concerning the routine use of gold-salt therapy in rheumatoid arthritis is still unsettled, we shall not discuss the regime in detail. We shall point out what seem to be pertinent generalizations as they apply to the selection of patients and their treatment and to the end results. The cases are used to illustrate our chart, not to defend or abuse gold-salt therapy in rheumatoid arthritis. The use of this treatment at the Robert B. Brigham Hospital has been, and still is, considered a research problem that is in progress.*

Case 1 (R. B. B. H. 1847) is that of a twenty-one-year-old stenographer with rheumatoid arthritis of twenty-one months' duration who was admitted for gold-salt therapy after a previous admission and follow-up study in the clinic. During the twenty-one months before the second admission, the patient had become progressively worse until she was barely able to get in a chair for part of the day.

FIGURE 2. *Chart of Case 1.*

DATE	A	D ₁	D ₂	I	C	T	LOCATION	REMARKS
6/25/40	3	3	2	3	2	1	Hospital	Second admission, arthritis 21 mo
7/10/40	3	3	2	3	2	1	Hospital	Before gold salts
9/23/40	1	1	2	1	1	0	Hospital	After gold salts
12/ 2/40	1	1	2	1	0	0	Home	3 mo. later
3/ 1/42	0	0	2	1	0	0	Working	18 mo. later

Figure 2 illustrates the course that this patient followed for the eighteen months after therapy. There was a satisfactory response, which has

*In the presence of essentially normal blood and urinary findings and in the absence of a history of kidney or liver disease or a sensitivity to drugs, these patients with active rheumatoid arthritis received one 25 mg. dose, one 50 mg. dose and nineteen 100 mg. doses weekly of a soluble intramuscular preparation (gold content, 50 per cent). This gave a total of 1975 mg. over a period of twenty-one weeks. Complete blood examinations, sedimentation indices and urinalyses were done weekly. All the patients were hospitalized for this therapy.

persisted. As a relatively early case, the objective measurements all improved except D₂, which measured the mechanical deformity of limitation of motion in the knees. Despite this deformity which is permanent, owing to fibrous-tissue adhesions and some joint damage, the patient has been able to become self-supporting (A), has no sign of disease activity in her joints (D₁), has gained weight (T), has lost her anemia (C) and is essentially a well person objectively except for the borderline abnormal sedimentation index (I) and the aforesaid mechanical deformity.

Figures 3 and 4 (Cases 2—R. B. B. H. 1910—and 3—R. B. B. H. 1917) represent the use of our curve in 2 other patients with active rheumatoid

FIGURE 3. *Chart of Case 2.*

DATE	A	D ₁	D ₂	I	C	T	LOCATION	REMARKS
11/ 7/39	2	3	2	2	1	3	Hospital	Admission, arthritis 43 mo
4/11/40	2	2	2	2	1	2	Hospital	Before gold salts
6/29/40	0	0	2	1	0	1	Hospital	After gold salts
2/ 4/41	0	0	2	0	0	0	Working	8 mo. later
3/ 1/42	0	0	2	1	0	0	Working	21 mo later

arthritis who were badly crippled because of the inflammatory aspect of the disease, but with some degree of mechanical deformity. The patient in Case 3, a fifty-nine-year-old woman, became active

FIGURE 4. *Chart of Case 3.*

DATE	A	D ₁	D ₂	I	C	T	LOCATION	REMARKS
3/23/40	4	3	2	3	2	4	Hospital	Admission, arthritis 6 mo
4/11/40	4	3	2	3	2	4	Hospital	Before gold salts
7/16/40	2	2	2	1	2	1	Hospital	After gold salts
12/19/40	0	0	2	0	0	0	Working	5 mo later
2/27/41	0	1	2	1	0	0	Working	7 mo later
5/10/41	4	3	2	3	2	2	Home	10 mo later

following a course of gold salts. However, ten months later the chart figures show a definite return of arthritic activity, for which a second course of gold-salt therapy is being administered.

It should be noted that in neither of these cases did mechanical deformity (D₂) improve, and that the rather temporary response in Case 3 may have been a spontaneous remission rather than the response to the gold medicament. Certainly the response in the second course of treatment has not been so dramatic as in the first.

Figure 5 (Case 4—R. B. B. H. 1803) shows what happened during the course of the second admission of a thirty-eight-year-old Italian housewife who received the routine procedures of good diet with extra vitamins, rest, physiotherapy, orthopedic devices and so forth for four months, with the only change in her chart a shift in A from 4 to 3. With gold therapy there was an appreciable change for the better. Despite what was definite improvement, certain numbers in the

chart that signify low-grade activity have persisted at a low level, and these have kept the patient's

FIGURE 5 Chart of Case 4

DATE	A	D ₁	D ₂	I	C	T	LOCATION	REMARKS
1/18/40	4	3	2	2	1	2	Hosp ital	Second admission on arthritis
5/5/40	3	3	2	2	1	2	Hospital	Before gold salts
7/30/40	1	1	2	1	1	1	Hosp ital	After gold salts
10/24/40	1	1	2	1	1	1	Home	3 mo later
3/1/42	1	1	2	1	1	0	Home	18 mo later

functional activity from becoming normal, although she is taking care of her family.

Case 5 (R. B. H. 1978) was that of a fifteen-year-old schoolboy with active rheumatoid arthritis (Still's disease). He did not respond to gold salt therapy, as shown by the chart (Fig 6), but did

FIGURE 6 Chart of Case 5

DATE	A	D ₁	D ₂	I	C	T	LOCATION	REMARKS
2/26/40	4	3	2	3	2	4	Hospital	Admission and referral 4 mo
9/6/40	4	3	2	3	2	4	Hospital	Before gold salts
12/18/40	4	3	3	3	2	4	Hospital	After gold salts
4/1/41	3	2	3	2	1	3	Hospital	4 mo later
7/1/41	3	2	2	2	0	2	Hospital	7 mo later
3/1/42	2	1	2	2	0	0	Home	15 mo later

undergo what was probably a normal remission some months after the end of therapy, and the chart then followed the same type of response as seen in patients who responded to gold salts. Here again, a large part of the mechanical deformity persisted, but subluxation (D₂) was corrected by vigorous orthopedic treatment. In this case seven months of routine therapy had produced no change for the better, as shown by the chart, and this was obvious from a clinical study of the patient, nor did gold therapy produce any real improvement. However, when a spontaneous remission occurred the chart portrayed the fact that the patient was improved enough to be allowed home to plan some vocational training.

Case 6 (R. B. H. 1899) portrayed in Figure 7, was that of a forty-year old man with marked mechanical deformity and a relatively low grade arthritis. There was no change after eight months

FIGURE 7 Chart of Case 6

DATE	A	D ₁	D ₂	I	C	T	LOCATION	REMARKS
10/24/39	3	2	3	2	1	2	Hosp ital	Admission and referral 36 mo
6/25/40	3	2	3	2	1	2	Hospital	Before gold salts
9/23/40	3	2	3	2	1	0	Hospital	After gold salts
12/2/40	3	2	3	2	1	0	Hospital	3 mo later
2/1/41	2	2	3	1	0	0	Hospital	5 mo later

of routine therapy. The change after gold salt therapy is illustrative of what occurs in patients with marked mechanical deformity who improve

with gold salts or spontaneously, usually over a long period of time. The objective measurements of inflammation or arthritic activity (D₁, I, C and T) changed in this patient for the better, but the joint damage was sufficient to cripple permanently or at least to handicap him.

The last case illustrates a general rule that we have found useful in selecting patients for different kinds of therapy. The patients who require medical care, such as bed rest, better nutrition, mild physiotherapy, resting shells and so forth, are those in whom D₁, I, C and T are high; this group should be considered for gold salt treatment. The patients in whom the mechanical deformity, not joint inflammation, is a main factor must be treated by vigorous physiotherapy, orthopedic appliances and surgery; gold salt treatment will not help this group. These two phases of the disease are represented in Case 6. Gold salt therapy, hand in hand with optimum general medical treatment, caused a relative disappearance of arthritic activity. Vigorous muscle exercises in bed and in the tank and the use of orthopedic appliances, such as iron calipers for the knees, then allowed the patient to improve his functional level (A) from "bed and chair" to "ambulatory—confined to one floor." This was possible despite the continued subluxation of the knees. Further orthopedic attack, such as arthroplasty of the knees, might improve the functional activity to a still better level.

Since the cases presented in this paper seem to have done well following gold salt therapy, we emphasize again that in Cases 1 and 2 the satisfactory response could be attributed to this form of therapy. Case 3 may well have had a spontaneous remission. Cases 4 and 6 improved only slightly during gold salt therapy, and in Case 5 there was no response to it. In addition, 3 of these patients showed minor toxic heavy metal effects, such as small ulcerations in the mouth and a slight dermatitis when exposed to the sun. A subsequent series of patients receiving smaller and consequently less toxic amounts have not shown marked changes in their charts.

SUMMARY

A simple numerical chart for use in studying the course of rheumatoid arthritis is presented. As its objective measurements are an indication of the presence or absence of arthritic activity, it can aid in determining the most useful therapeutic approach for a particular patient.

The use of the chart as a therapeutic yardstick for the response or lack of response of rheumatoid arthritis to gold salt therapy is illustrated by case reports.

MEDICAL PROGRESS

NEUROLOGY

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SO MANY topics pertaining to neurology have appeared in earlier Progress Reports that it is difficult not to duplicate. With an attempt to avoid duplication or with approach from a different angle, a miscellaneous group of subjects for discussion has been chosen, which I have found of interest and which may not be too old a story for the reader.

REACTION OF NERVOUS SYSTEM TO SULFONAMIDES

Reactions following the use of three sulfonamide drugs were listed in 1941 in a circular letter of the National Research Council.¹ Besides the relatively common effects on the blood and kidneys, the following concerned the nervous system:

EFFECT	SULFANILAMIDE	SULFAPYRIDINE	SULFATHIAZOLE
Nausea and vomiting.	Fairly common	Frequent	Uncommon
Dizziness	Common	Common	Uncommon
Psychosis	0.6% of cases	0.3% of cases	Very rare
Neuritis	Very rare	Not reported	Rare
Ocular or auditory . .	Rare	Rare	Rare

Since this report sulfadiazine has come into common use. In their report on the Halifax epidemic of meningococcal meningitis, in which a phenomenal therapeutic success was registered, Dingle et al.² state that nausea, vomiting, dermatitis, cyanosis or mental symptoms attributable to the drug were not present. Finland et al.³ in a paper concerned largely with the toxic effects of sulfadiazine give their conclusions based on 446 cases. They find the toxic symptoms from this drug to be "relatively mild and infrequent," although nausea and vomiting did occur in 9 per cent of cases. There was no note on a deleterious effect on the central or peripheral nervous system. A second paper emanating from the same source,⁴ and concerning a group of 460 patients treated with sulfadiazine, states that toxic reactions on the nervous system were limited to 2 patients. One of these was an alcoholic with pneumonia who showed delirium on the seventh day of treatment; the drug was stopped, and when given again three days later the delirium did not recur. The other patient was

disoriented and confabulated on the third day of treatment after taking 18 gm., with a blood level of 16 mg. per 100 cc. On the stopping of medication the symptoms cleared. No patient developed peripheral neuritis.

In a recent exhaustive study on the sulfonamides, Janeway,⁵ although listing the above nervous symptoms, implies that they have been reduced since the advent of sulfadiazine. However, he adds one more symptom to the list when he states: "An important practical point is that an ambulatory patient taking sulfonamides should be warned that his reaction time may be slowed. Special care should be observed in driving a car, crossing streets and performing manual work." This writer, with others, mentions two important points to be kept in mind concerning the development of toxic symptoms of any type: hypersensitiveness to the drug, either natural or following the previous use of a sulfonamide, and the late insidious development of toxic symptoms, sometimes even after the drug has been stopped. This second warning is especially directed to sulfadiazine because, as Janeway states, it produces severe reactions less frequently than sulfathiazole and is treacherous because of its slow excretion.

A case with a fatal outcome well known to me⁶ illustrates the insidious advent of toxic reactions in a patient probably sensitized to sulfa-drugs. This patient, a healthy although mildly hypothyroid woman of fifty-nine, was given sulfathiazole for urinary infection and later, because of unexplained fever, sulfanilamide, which was later changed to sulfadiazine; a total of approximately 30 gm. of all three drugs was administered. She then rapidly lapsed into a lethargic state, which continued until death two weeks later. During this period somnolence was the cardinal symptom, from which the patient could be awakened for a few minutes only, when she would recognize attendants and relatives. Although somewhat disoriented she could hardly be considered otherwise psychotic, offered no complaints except excessive fatigue, and showed no neurologic signs. Post-mortem examination revealed characteristic sulfonamide nephrosis. The brain was grossly normal, but micro-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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scopic examination showed diffuse toxic effects on both nerve cells and neuroglia.

Peripheral neuritis and spinal-cord lesions have been reported. Bieter et al.⁷ cite 2 cases of the former from sulfanilamide, and also mentions experimental injections in chickens following which peripheral neuritis ensued, and a case reported by Tolosa and Savoy.⁸ Ornsteen and Fürst⁹ found a neuritis with a distribution like that of progressive muscular dystrophy following the ingestion of 130 gm. of sulfanilamide in the course of thirty-five days. Elkington¹⁰ reports serious peripheral nerve damage following the intramuscular injection of sodium sulfapyridine, and naturally warns against its use in proximity to nerves. Cerebral symptoms simulating those of acute meningitis are described by Johnstone and Forgacs¹¹ from sulfapyridine, and a hemorrhagic encephalopathy was seen by Roseman and Aring¹² from the use of sulfamethylthiazole.

Several papers concern acute visual disturbance during the course of treatment by sulfonamide drugs. Blankstein¹³ attributes his case to an acute myopia, due, he believes, either to allergy or to a difference in osmotic tension of the lens as compared with the aqueous humor produced by the unequal distribution of sulfanilamide within the eye.

Little¹⁴ lists the following nervous and mental complications that have been reported: dysmorphismia, aphasia, agraphia, stammering, toxic psychosis, peripheral neuritis, encephalomyelitis, myelitis, optic neuritis, transitory myopia, meningeal signs, blindness and convulsions. Such an array of serious by-effects is at first startling, but it should be remembered that these complications occurred with sulfonamide drugs now abandoned, and in dosages that are no longer acceptable. Against this implication that sulfonamide drugs are extremely toxic to the nervous system is the experience of Finland, already mentioned, with 906 patients treated with sulfadiazine in only 2 of whom nervous-system symptoms developed. Little himself, although listing these serious effects, makes some explanation when he says, "The drugs appear more neurotoxic in the presence of pre-existing disease of the nervous system." He also states, as does Janeway, that the intermittent administration of a single sulfonamide or successive administration of different sulfonamides seems to predispose to the development of toxic nervous-system symptoms.

In conclusion, mild and severe toxic symptoms referable to the nervous system must be recognized as ever-present possibilities, especially if the patient has latent or declared disease of the brain or spinal cord. However, with care as to the choice of drug and dosage serious sequelae can usually be avoided.

LOCAL USE OF SULFONAMIDES WITHIN CRANIUM

The neurosurgeon would like to have a safe antiseptic to apply locally or over the dura, either as prophylaxis or in the presence of infection, and it is natural that he should wish to use a sulfonamide drug that theoretically should be effective against the bacteria ordinarily encountered.

If one is familiar with the history of numerous liquid antiseptics that have been injected into the subarachnoid space, both in animals and in man, in different types of meningitis and also in uninfected laboratory animals, he will approach the subject with great skepticism. The conclusions forced on the older investigators—for the subject has been generally banned for years—were that all antiseptics did harm and no good.¹⁵ But the sulfonamide drugs are not antiseptics comparable to corrosive sublimate, lysol and so forth, and perhaps this prejudice is unfounded. I have myself used penicillin intracisternally in pneumococcal meningitis, without apparent harm.

Present interest concerns the toxicity, irritability and usefulness of sulfonamide powders placed directly on the brain cortex and over the dura, and there are at hand four reports using apparently similar technics, but with disagreement concerning results. Watt and Alexander¹⁶ applied sulfathiazole powder epidurally in the case of 6 frontal craniotomies. In 5, epilepsy occurred promptly. In the remaining case, in which epilepsy did not appear, the dura at this point had not been opened. The conclusion seemed obvious that seepage of the drug through the dural opening was the cause of the epilepsy. Experiments on cats substantiated the results in man. Other sulfanilamide drugs so used did not produce epilepsy, nor did sulfathiazole used similarly but in posterior craniotomies cause epilepsy.

Pilcher et al.,¹⁷ experimenting with cats and rabbits, placed sulfathiazole powder directly over the cortex and closed the dura over it. In 36 animals almost all had focal epileptic seizures, which became generalized. Fits were not produced by sulfadiazine or kaolin used as a control, and only once by sulfanilamide. At autopsy weeks or months later the drugs were found in hard plaques adherent to the cortex. At no time did the drugs appear in the blood or spinal fluid in appreciable amounts.

These two papers are in essential agreement that epilepsy results from the local use of sulfathiazole powder when placed on or near the cerebral cortex.

Hurteau^{18, 19} placed various sulfonamide drugs in small, aseptically prepared wounds of the cortex and subsequently covered the wounds with dura. He does not mention epilepsy as resulting from

these experiments. On examination he found little reaction of the brain or meninges; well preserved nerve cells could be seen near the margin of the wounds, and there was minimal meningeal reaction. The rate of absorption was most rapid with sulfanilamide and slowest with sulfapyridine; with sulfathiazole and sulfadiazine intermediate.

Ingraham and Alexander²⁰ superficially traumatized the cortex in 7 cats and 3 monkeys, some with aseptic and some with nonsterile technic. Powders of sulfanilamide, sulfathiazole and sulfadiazine were applied to the traumatized cortices and the animals were killed in three to five weeks. Epilepsy was not observed. In general there was surprisingly little reaction to the drugs.

It is obvious that with such contradictory results much more work will have to be done before the local use of sulfonamide drugs can be considered either safe or advantageous.

MYASTHENIA GRAVIS

Operative removal of the thymus gland as a cure for myasthenia gravis has recently received considerable notice, especially since the publication of the paper of Blalock et al.²¹ in 1941. It has been suspected for many years that there may be a relation between the thymus gland and myasthenia, because of the finding of an enlarged gland or a thymic tumor in this disease at autopsy. Poer²² states that in a total of 129 autopsies and operations in myasthenic cases enlargement of the thymus gland was found in 71 cases, an incidence of 55 per cent. In 1939 Blalock et al.²³ reported a case that was said to be the "fifth instance of an attempt to influence the course of myasthenia by an operation on the thymus." This was a removal of a cystic tumor. The patient was reported as entirely well four years later. Since then Campbell²⁴ has removed two thymomas, one a large cystic tumor, the patient doing well two years after operation but still taking Prostigmine. Turnbull²⁵ removed a malignant thymoma without benefit, and Poer²² a malignant thymic tumor with improvement over a period of four months.

Encouraged by success in the removal of a cystic tumor, Blalock et al.²¹ turned to another aspect of the subject. Removal of thymic tissue in which no tumor could be discovered was carried out in 6 cases. In 5 of these, definite hyperplasia was present, but no tumor. The early results were gratifying, but an addendum to this paper states that only 3 of the 6 patients continued to show improvement from the operation.

Four patients chosen with care because of constancy of symptoms have been subjected to thymectomy at the Massachusetts General Hospital.

No tumors were expected and none were found. The results have so far not been encouraging.²⁶

In appraising the value of operations on the thymus gland for myasthenia gravis, one must clearly distinguish between three conditions: malignant tumors of the gland, hypertrophy, and degenerative states and remnants. As pathological classification is as yet not too clearly defined, and physiologic tests for the function of thymic tissue are not yet available, the effect of thymus-gland excision cannot at present be properly evaluated. Thus far the most striking improvement in the course of myasthenia has been reported from excision of cystic and malignant thymus glands, the excision of the normal or hypertrophied gland still awaits evaluation, and that of thymic remnants seems to offer the least benefit. Further operations must precede a proper conception of the thymus gland in relation to myasthenia gravis.

X-ray therapy of enlarged thymus glands was at one time recommended. In 1923 Mella²⁷ published the report of such a case. A woman of twenty-three presented herself with progressive difficulty in swallowing, chewing and speaking. A typical myasthenic reaction to faradism was obtained. X-ray disclosed a precardiac shadow that was considered consistent with an enlarged thymus gland. Thirteen months after the onset of symptoms, at this time incapacitating, x-ray treatment was inaugurated, the patient receiving four suberythema doses at three-week intervals, directed to the thymus gland. In five weeks she was much better; in one year she was well and working, and electrical reactions were normal. This patient returned to the hospital four months ago, twenty years after her first admission, because of another complaint; she was free from all myasthenic symptoms. Further evidence that the diagnosis was probably correct was given by her; four years previously immediately following a pelvic operation under spinal anesthesia she had experienced a transitory drooping of the eyelids and difficulty in swallowing and talking. In this case there was only x-ray evidence of a shadow in the region of the thymus gland, which was said to have disappeared after x-ray therapy. The symptoms were highly suggestive of myasthenia gravis, and after persisting for more than a year disappeared following x-ray treatment. It seems reasonable to entertain a probable relation between the thymus gland and myasthenic symptoms.

Pregnancy has been thought to affect the course of myasthenia gravis. Sometimes it is said to produce relapse and sometimes remission. Viets et al.²⁸ in their large and well-controlled series present 8 cases in which remission during pregnancy was the rule, making possible a reduction in medica-

tion or even discontinuance of the drug. Improvement usually began soon after conception and lasted until well along in the puerperium. Rarely an increase of myasthenic symptoms occurred, if so, it was early in the course of pregnancy and was not severe. These authors believe that pregnancy, labor and nursing do not affect the course of the disease unfavorably, and they do not advocate early abortion, as has been advised and practiced by some.

In this connection there is an extremely interesting report of a myasthenic baby born of a myasthenic mother.²⁹ As in Viets's cases, the mother, whose condition conformed in every way to the diagnosis of myasthenia gravis, went through pregnancy without incident, although it was necessary to increase the dose of Prostigmine slightly. The baby weighed seven pounds, eight ounces, at birth and appeared well formed and normal until the third day, when difficulty was experienced in taking its formula. On the fourth day its face was masklike, the jaw drooped, the cry was almost noiseless, and mucus collected in the throat. The response to 4 mg of Prostigmine in milk was dramatic, all symptoms disappeared and the baby nursed normally. In spite of persistent use of Prostigmine sudden death occurred on the seventh day after birth. So far as known, this is the first case suggesting the hereditary transmission of myasthenia gravis.

The age of onset of symptoms of myasthenia gravis has been set much earlier than previous statistics indicated. Although commonly recognized as a disease of youth and young adults, ten years is usually considered the low limit of age. The case just quoted, showing myasthenic symptoms at birth, and another case³⁰ with onset at five years change the conception of the age incidence. That myasthenia gravis is not only hereditary but also familial is suggested by Riley and Frocht,³¹ who report two sisters with onset at eleven and fourteen years respectively. The disease has usually been considered neither hereditary nor familial.

Although the importance of the Prostigmine test in the diagnosis of myasthenia gravis is now a matter of common knowledge, it may well be called to mind again for there are numerous other conditions manifesting muscular weakness that are easily confused with it. As time goes on, the prompt improvement seen on administering this drug in myasthenia gravis is so dramatic that Prostigmine may well be considered specific. In no other disorder does one see more than slight benefit, and in some conditions, notably bulbar paralysis, exaggeration of the paralysis may occur. It is well therefore to emphasize the Prostigmine test elaborated by Schwab and

Viets³² as a diagnostic test for myasthenia gravis. The test consists of a point scale estimate of objective and subjective improvement in the various symptoms before and after the intramuscular injection of 15 mg (1/40 gr) of Prostigmine Methylsulfate and 0.6 mg (1/100 gr) of atropine—ampules containing these amounts and marked for diagnostic use are obtainable. Examinations are made every ten minutes for an hour, and improvement is recorded on a scale ranging from "1" to "5." As stated above, this test may be dangerous in bulbar palsy, because of increased difficulty in breathing and choking. It should therefore not be used at all in such cases, or the dose should be smaller than otherwise.

METASTATIC CANCER

It requires an enthusiast to discuss metastatic cancer in any location, particularly when the tumors lie within the cranial cavity or the spine. Patients so afflicted are the despair of relatives and physicians alike, for the inability to bring to them any useful therapy—other than morphine—is the general rule. Even textbooks on neurology pay scant attention to these cases, and yet they offer a constant challenge in differential diagnosis. Experience shows that metastasis to the brain is often mistaken in its early stage for a vascular accident, encephalitis or some other disease. Even though a primary malignant growth is found elsewhere in the body, it is not sound reasoning to assume that coexisting cerebral symptoms must also be due to metastasis. It is, of course, recognized that the lung is the seat of primary or secondary malignancy that ultimately finds its way to the brain, yet how often one forgets to study the lung for this evidence, and how often one fails to find it when it is looked for. Although not certain in its diagnostic role, x-ray examination of the lung usually shows a shadow characteristic or at least suggestive of carcinoma, and it is now a rule, sometimes forgotten because of lack of pulmonary symptoms, to call in this evidence in suspected brain tumor.

Carcinoma of the lung and brain metastasis. One of the commonest types of brain metastasis is that derived from bronchogenic carcinoma. It is also a type frequently mistaken in its early period, for two chief reasons: because the early symptoms are not usually characteristic of tumor of the brain, and because pulmonary symptoms are either minimal or absent and x-ray signs are noncommittal. A review of this subject by King and Ford³³ is therefore welcome. Of 100 cases studied at the Johns Hopkins Hospital and coming to autopsy, 27 showed metastasis to the central nervous system. The age incidence was forty to sixty years; the sexes

were equally distributed. Metastasis to the brain occurred early, and in 14 cases cerebral symptoms dominated the clinical picture, antedating the pulmonary symptoms. The lesions found were usually multiple and small, the cortex, white matter, brain stem, hypothalamus, cerebellum and meninges being indiscriminately the seat of invasion. Less commonly a large solitary tumor (4 cm. or more in diameter) was found. Initial symptoms and signs were of two general types; more commonly they were mild and indefinite in character and location and were associated with mental disturbance, but not infrequently a rapid onset suggestive of embolus, thrombosis or hemorrhage, was noted, and occasionally the first symptom was a convulsion followed by hemiplegia. Although headache was usually present, papilledema was rare, occurring in only 5 of the 27 cases, and the spinal fluid generally failed to show elevation of pressure, although increase in fluid protein was the rule. X-ray films of the skull were negative except in the event of bone involvement.

Globus and Meltzer³⁴ have recently analyzed 57 cases in which autopsy revealed metastatic growth. Many of their statistics are worth while having in mind for the purpose of differential diagnosis. These authors found a percentage of metastatic lung cancer even higher than is generally supposed. Of 33 cases where complete autopsy was available, 19 were from this source. The fact that in 49 of the 57 cases the brain showed carcinomatous metastasis is no surprise, but that metastasis was single in 39 per cent of all cases is contrary to the general impression. On the clinical side, Globus and Meltzer emphasize the well-known fact that papilledema is usually absent or only of moderate degree and that spinal-fluid examination is seldom helpful.

For the clinician these two papers are extremely helpful, for the early manifestations of metastatic tumor of the brain are seldom clear cut. Especially must one be reminded to examine the lungs with great care in patients suspected of having brain tumor.

Carcinoma of prostate and metastasis to spine. The feeling of helplessness in the presence of metastatic cancer has at last been tentatively relieved by the dramatic effect of orchidectomy on carcinoma of the prostate. Although the general subject has recently been treated in these reviews by Quinby,³⁵ it is perhaps not amiss to emphasize the beneficial effects of this procedure on the pain of nerve-root involvement, and to add a note on a case known to me.

The beneficial effects of orchidectomy and of diethylstilbestrol on carcinoma of the prostate have during the past year been the subject of more than

one symposium of urologists. In particular the papers of Huggins and his associates,³⁶ Alyea and Henderson,³⁷ Chute, Willetts and Gens³⁸ and Nesbit and Cummings³⁹ and discussion by various surgeons may be cited as in general agreement that orchidectomy causes an involution of carcinoma of the prostate, and where metastasis to the spine is present prompt relief of pain occurs. For the most part there is general agreement that bony metastases in the spine and pelvis also regress, and x-ray evidence of the healing of such lesions is offered. There is a difference in opinion whether to employ diethylstilbestrol before or along with castration, and the relative merits of the operative as compared with the hormonal effect on the tumor are not yet settled.

None of the writers mentioned deal with the subject from a neurologic point of view; they do not state whether the metastasis was limited to the spine or to the intervertebral foramina, or was intraspinal. In a case known to me the metastasis was shown to be definitely within the spinal canal. Relief from pain and removal of the spinal-fluid block, first after diethylstilbestrol medication, and subsequently as a result of castration, gave objective evidence of the beneficial effect of both these therapeutic agents on an intraspinal tumor. The following abstract of this case, reported by Clarke and Viets,⁴⁰ is instructive:

A 69-year-old man had noted pain in the legs and difficulty in walking for six months. Physical examination revealed tenderness over the lumbar spine, lumbar lordosis, absent knee and ankle jerks and an enlarged prostate, a needle biopsy of which showed carcinoma. X-ray films gave evidence of metastasis to the lumbar spine. Lumbar punctures at the lowest dorsal and lowest lumbar levels showed partial dynamic block, and the fluid from the lower puncture contained 798 mg. of protein per 100 cc. Four days after the beginning of diethylstilbestrol therapy the patient was free from pain and ambulatory, and 8 days later the spinal-fluid dynamics and protein and the neurologic findings had returned to normal. He returned to work, and 11 weeks after the beginning of therapy the prostate had diminished in size and another lumbar puncture showed no evidence of block and a normal spinal-fluid protein. The diethylstilbestrol was discontinued. The patient continued work for 4 months, when the pain and difficulty in gait returned and lumbar puncture revealed complete dynamic block and a protein of 7500 mg. per 100 cc. in the spinal fluid from the lower needle. Orchidectomy was performed, and 5 days later the symptoms were completely relieved. Twelve days later the spinal-fluid dynamics were normal and the protein was 80 mg. per 100 cc. When last seen, 6 weeks after operation, the patient was free of pain.

Sufficient time has not elapsed to estimate the late effects of this treatment. Even if a long-time cure is not forthcoming, the immediate effect is far

better than was possible by neurosurgery, x-ray therapy or medication. Furthermore, a line of hopeful research has been opened into the pathogenesis of other forms of malignant disease.

THYROTOXIC MYOPATHY

Thyrototoxic myopathy, an unusual condition, but one in which the unfortunate diagnosis of progressive muscular atrophy is apt to be made, is discussed by McEachern and Ross.⁴¹ Although rare, this syndrome should be recognized early, as a cure may be expected from treatment, and unrecognized cases go on to death.

These authors analyze 13 cases—10 from the literature and 3 of their own. The similarity of the clinical picture in all cases is striking, and may be described succinctly as that of toxic goiter in addition to an exaggerated state of progressive muscular atrophy. The patients are usually middle-aged men who present themselves complaining of excessive fatigue and loss of weight during a period of weeks or months. Most conspicuous is generalized muscular wasting associated with gross muscular twitching. The patient also perspires freely, runs a rapid pulse, and shows a fine tremor of the outstretched hands—this in addition to the muscle fasciculation. There may or may not be exophthalmos and enlargement of the thyroid gland. The basal metabolic rate is elevated, but not excessively so (+14 to +68 per cent in 12 cases, +100 per cent in 1 case). Favorable response of all symptoms to Lugol's solution and thyroidectomy is rapid and complete, as was shown in 10 cases. The 3 patients not operated on died, 2 of respiratory paralysis.

Although there is a close resemblance between thyrototoxic myopathy and progressive muscular atrophy, complete restoration of function and the disappearance of all signs under treatment militates against the presence of a disease of the central nervous system. Examination fails to show the neurologic signs associated with progressive muscular atrophy or amyotrophic lateral sclerosis. McEachern and Ross offer some evidence that the locus of weakness and fasciculation is at the myoneural junction, as follows: the patients complain of rapid loss of strength on action, as in myasthenia; Prostigmine abolishes weakness temporarily, as in myasthenia; and injection of the nerve with novocain does not stop the fasciculation of the appropriate muscle.

These authors refer to a case reported by Ayer, Means and Lerman.⁴² This patient closely resembled others of the series analyzed by McEachern and Ross. He improved promptly following partial thyroidectomy and worked regularly for five

years, when he developed pulmonary tuberculosis. Neurologic examination at that time was negative except for slight, fine tremor of the hands. The basal metabolic rate was -8 per cent, as against +60 per cent previously.

Another patient of this type was seen by me in 1939. He also recovered as a result of thyroidectomy, and was working as a mechanic more than two years afterward.

This disorder is undoubtedly rare, but should be recognized because of the fatal outcome that has been seen in untreated cases. With Lugol's solution and with thyroidectomy recovery is to be expected. As most patients present themselves within a few months of onset of weakness and rapidly progressive loss of weight, the illness should preferably be termed "acute" or "subacute."

TREATMENT OF CAROTID ANEURYSM

The treatment of carotid aneurysm is an old topic, but recent papers make revision reasonable at the present time. The subject may be approached more intelligently if the following conclusions are admitted: Aneurysms of the brain are of common occurrence; for the most part they are untreatable by direct attack; but some, notably those involving the internal carotid arteries, can be successfully treated indirectly by surgery.

It may not be entirely sound on grounds of etiology or pathology to separate one type of aneurysm from another, but in most cases it is possible to state which are operable and which are not. Generally speaking, the commonest type of aneurysm is small, occurs especially at the junction of arteries composing the circle of Willis, and after an indefinite period may rupture spontaneously. Some authors think that these aneurysms arise from a congenital defect in the tunica elastica, but they have been found in many people well beyond youth or even middle age. When these military aneurysms rupture there is an outpouring of blood into the subarachnoid space, usually filling the basal cisterns and the spinal subarachnoid space, from which it is recovered by lumbar puncture. The symptoms are primarily those of an acute meningeal irritation, with or without focal cerebral or cranial-nerve signs. As a common site of this type of aneurysm is at the junction of the middle cerebral and posterior or anterior communicating arteries of the circle of Willis, the third nerve is often involved and pressure paralysis results. This location is nearly the same as that of saccular aneurysms, to be discussed later. Military aneurysms have been described by pathologists and clinicians in many papers during the past decade, and almost every physician will recognize this type

of aneurysm. Treatment is still a matter of debate, but no one has described a method of direct surgical intervention. Without specific treatment the outlook for recovery is good in approximately 50 per cent of cases.⁴³

As contrasted with these minute aneurysms, there are the less frequent saccular ones. They are usually found in the large intracranial arteries, the basilar and internal carotid arteries in particular. That they have a different origin from miliary aneurysms is suggested by the fact that they do not commonly occur at arterial junctions, that they grow to a large size before rupturing, and that they are often associated with arteriosclerosis. One or two characteristics are held in common between miliary and saccular aneurysms. Neither seems to be caused by syphilis, and in neither do symptoms appear before rupture, so long as the saccular aneurysm remains small. But here the analogy ceases, for when a saccular aneurysm enlarges it does produce symptoms by pressure on neighboring structures; this is particularly true of the saccular aneurysms of the internal carotid artery, and in these surgery must be considered.

From the foregoing remarks, it appears that from the surgical therapeutic point of view the primary concern is with saccular aneurysms of the internal carotid artery in its intracranial course. The diagnosis can hardly be made until the aneurysm is large enough to produce pressure symptoms, and even then must be differentiated from tumors occupying the same site. If the patient or his physician hears a bruit, aneurysm is of course suggested, but a bruit is rare except in the case of arteriovenous aneurysms, which is not the subject of the present discussion. A favorite site for an expanding internal carotid artery is in its course at the border of the cavernous sinus, and in this region four cranial nerves are in immediate proximity, the third, fourth, fifth and sixth. Jefferson⁴⁴ has given clear-cut anatomical localization for this subclinoid type of carotid aneurysm, of which he found 16 in a series of 55 cases of intracerebral aneurysm. Utilizing the four cranial nerves mentioned, he localizes the site of aneurysmal dilatation in the three following categories:

Group A. Posterior Cavernous Syndrome.—Three divisions of trigeminus affected, with ocular palsies, sometimes only abducens; motor root of trigeminus usually affected, but may escape.

Group B. Middle Cavernous Syndrome.—First and second divisions of trigeminus affected, third spared; paralysis of one nerve, but usually of all nerves, supplying muscles of eye.

Group C. Anterior Cavernous Syndrome.—First division of trigeminus affected, other divisions spared; paralysis of superior division of the oculomotor nerve or of all nerves supplying muscles of eye.

It will be seen from the above schema that localization depends much on the amount of pressure exerted on the trigeminal roots.

Aneurysms may also develop in the internal carotid artery above the cavernous sinus and before the artery joins the circle of Willis. These supraclinoid aneurysms cause an entirely different compression syndrome from that of subclinoid aneurysms. In such a case the optic nerves, chiasm or optic tracts are pressed on, producing visual-field defects. Pituitary function may be disturbed so that an endocrine picture is presented similar to that of pituitary tumor. A number of such cases have been operated on and an aneurysm disclosed, to the embarrassment of the surgeon.^{45, 46}

Objective aid in the diagnosis of carotid aneurysm may be obtained from x-ray examination of the skulls. The most significant findings are erosion of the clinoid processes of the sella turcica on the appropriate side and concentric calcification within the aneurysmal wall. Moreover, the aneurysm may be clearly delineated by thorotrast injection, as advocated by Moniz.⁴⁷

Treatment should obviously be directed to reducing the size of the aneurysm or of doing away with it altogether. As the latter is technically impracticable one can only limit the amount of blood reaching the aneurysm, and for this Jefferson⁴⁴ offers three general procedures: occlusion of the common carotid artery, partial or complete ligation of the internal carotid artery in the neck and ligation of the carotid artery intracranially. He does not clearly commit himself concerning which procedure he favors, but one gathers in reading his papers that he is often satisfied with tying off the common carotid, which only partially reduces the blood reaching the brain via the internal carotid on the same side. Dandy⁴⁸ prefers to clip the vessel intracranially. It is a little difficult to estimate the value of these procedures, because the natural evolution of aneurysm appears to tend toward its occlusion, at least in some cases. Jefferson⁴⁴ describes such a case. Unexpectedly he uncovered an aneurysm in this location and withdrew; the patient recovered sufficiently to lead an active life for fourteen years. Seven years after the operation, x-ray examination suggested that the aneurysm was grossly calcified. Moreover, it is common knowledge that without ligation there may be no advance in symptoms over long periods of time, and since ligation seldom clears up existing symptoms, the results of a waiting policy and of ligation may be the same. If one could be sure that carotid ligation would prevent subsequent hemorrhage, this alone would be an indication for operation, but even this cannot be taken for granted.

Operative attack on the aneurysm itself is not recommended by anyone, although Dandy⁴⁹ was fortunate in removing a large aneurysm arising from the anterior cerebral artery, mistaken for tumor. When aneurysms have been opened through error the surgeon is usually pleased if he can retire without lethal bleeding.

Much has been said concerning the dangers of ligation of the internal carotid artery, and this subject has been carefully studied by Schorstein,⁵⁰ who collected 60 cases of aneurysm from the literature for statistical review. He divides them into three groups: infracaloid (22 cases, no deaths); supracaloid without leakage (22 cases, 3 deaths); and supracaloid with leakage (12 cases, 5 deaths).

The principal complication following carotid ligation is hemiplegia, sometimes immediate and sometimes delayed. A variety of causes for such a serious complication have been entertained, namely, thrombosis by extension, embolism from a supposed thrombus distal to the ligature, and anoxemia from cutting off too much of the blood supply of the circle of Willis. Schorstein finds the evidence strongly in favor of simple ischemia, and concludes that it is the patency of the circle of Willis and general systemic blood pressure that determine whether or not ligation will lead to hemiplegia and death. Dandy⁵¹ has performed 88 ligations of the internal carotid artery—partial ligation in the neck in 25 cases, total in the neck in 36 and intracranial clipping in 27. In all he observed immediate cerebral complications in 4 cases and late cerebral complications in 1 case, with 4 deaths. As a preventive he recommends the Matas procedure of intermittent digital compression of the carotid artery for two weeks prior to ligation, in order to improve collateral circulation through the circle of Willis.

It is difficult to summarize the subject because each case presents two unknown components of vital importance, that is, the exact size and condition of the aneurysm, and the patency of collateral circulation through the circle of Willis. If the latter is sufficient and if the general cardiovascular system is intact, ligation of the carotid artery, external or internal, is probably safe. Digital compression of the carotid should be used to check this. In selected cases, ligation can be expected to reduce the size of the aneurysm; in some cases it facilitates its obliteration and improves pressure symptoms, although seldom causing them to disappear. The above conclusions appear to be correct for all aneurysms of the internal carotid artery arising within the skull, but are especially applicable to those situated low, in or near the cavernous sinus.

TOXOPLASMIC ENCEPHALITIS

It is a question whether the practitioner of medicine will feel relieved at the recognition of another type of encephalitis. Time was when a case presenting acute cerebral symptoms of a diffuse character, in which bacteria could not be found or some poison could not be suspected, was labeled "toxic encephalopathy." In the last two decades, ever since the advent of the world-wide epidemic of acute encephalitis lethargica of 1917-1919, to be exact, considerable progress has been made, first in separating encephalitides from other types of cerebral lesions, such as vascular disease, tumor and abscess, and secondly in differentiating types of encephalitis. Yet even now it is difficult to define the term "encephalitis" or its associated spinal-cord term, "myelitis." Lest one think that the knowledge of the subject has made great strides, reference should be made to the paper of Adler,⁵² who studied 100 cases in which there was a diagnosis of acute encephalitis. Because of autopsy findings or subsequent course the diagnosis had to be revised in 30! This was in 1940. Nevertheless, of the large and diverse group of diseases that are spoken of as primary encephalitis, Webster⁵³ was able to say in 1941 that nine types have thus far been shown to be due to viruses with a special predilection for the central nervous system. When one remembers the 1917-1919 epidemic, the epidemic of St. Louis encephalitis of 1933-1934 and the recent epidemic of equine encephalitis, one cannot help but be interested in the subject and greatly concerned for the future, for however much has been learned of the nature of the different viruses, there is as yet no planned treatment and only partial preventive measures, and wars and depressions are breeders of encephalitides.

The present section deals with another type of encephalitis, proved to be due to the protozoan *Toxoplasma*. During the last five years a series of papers have developed the knowledge of this disease, and now Cowen, Wolf and Paige⁵⁴ have assembled the cases and have described a distinct clinicopathological entity. From that article the following description of this disease is summarized.

The lesion is produced by the protozoan *Toxoplasma*, which is found in the cerebrum; it is associated with the formation of miliary granulomas with reactive gliosis and fibrosis, especially in the brain-cortex, basal-ganglia and periventricular areas. Large areas of necrosis result, which become calcified. The lesions have been found especially in young children and babies, and in 1 case a stillborn infant presented the full-blown picture of the disease, indicating that toxoplasmosis is congenital. Curiously enough, the mothers could

not be shown to be infected, although neutralization tests on their bloods were positive. Various mammals, and perhaps birds, are probably the animal reservoirs of the infection, but the mode of transmission to man is not yet known.

In these babies supposedly infected in utero, signs of the disease, such as ocular disturbances, notably strabismus and abnormal movements of the eyes, naturally appear early. In 8 patients, signs were seen during the first four days of life. Convulsions, focal or generalized, as well as hydrocephalus, were often early symptoms, and both of these persisted if the patient survived. Those living long enough presented mental retardation and behavior problems.

The most striking and frequent ocular signs were those observed in the eyegrounds. Of 11 patients examined ophthalmoscopically, 10 showed chorioretinal lesions, with pallor of the optic disks. Another constant sign was the demonstration by x-ray of calcium deposits, already mentioned as occurring in areas of necrosis in the brain, usually in multiple foci. The spinal fluid and the ventricular fluid were abnormal, both being xanthochromic and showing an increased number of cells, thought to be lymphocytes, and also elevated protein levels.

A number of symptoms and signs not referable to the nervous system were present, such as splenomegaly and hepatomegaly, vomiting, diarrhea and edema of the extremities. Blood and spinal fluid injected into mice and rabbits intracerebrally and intraperitoneally produced toxoplasmosis. Neutralizing antibodies could be demonstrated in the blood.

The authors quoted are concerned with infantile, probably congenital, toxoplasmosis, the subjects dying early or in childhood. Pinkerton and Weinman⁵⁵ describe a case in a man of twenty-two who ran an acute course and died on the twelfth day. Sabin⁵⁶ reports 2 children, six and eight years old, also with acute febrile illness, one dying and the other recovering. These 3 cases presumably represent a different—acquired—type of the disease. Finally, there is the report of two much older people, one fifty years of age, the other forty-three, who ran the course of an acute illness and died on the fifth day, the other on the twelfth. In one of these cases the parasites were demonstrated in focal areas of encephalitis, and inoculation of this material into guinea pigs and mice reproduced the disease.

TOXIC EFFECTS OF DILANTIN SODIUM

Since its introduction as an anticonvulsant, Dilantin Sodium (sodium diphenyl-hydantoinate) has become one of the reliable drugs used in epilepsy at least in this country. Toxic symptoms

were described early in its use by Merritt and Putnam,⁵⁸ who introduced the drug into practice, and physicians are aware of most of these ill effects. Few have had the experience of Finkelman and Arieff,⁵⁹ who treated 44 patients with Dilantin and were forced to drop it in all except 7 cases because of toxic symptoms. They list thirty-one symptoms in all, the most commonly observed being ataxia, nystagmus, apprehensiveness and irritability, visual disturbances, tremors, electrocardiographic changes, nausea and vomiting, weight loss and gingivitis. They somewhat grudgingly admit that the 7 patients were continued on this treatment because they responded favorably to Dilantin when they had not done well under phenobarbital, bromides or both combined.

Rosenbaum⁶⁰ discusses this paper. He questions the implication that a number of the symptoms listed were due to Dilantin, and in particular he takes exception to the use of a paper published by him⁶¹ as evidence of dangerous toxic effects of Dilantin. He had described a boy who took sixty to seventy capsules, or 6 to 7 gm., of phenytoin sodium in ten hours as a suicidal attempt. Severe toxic symptoms developed, but the patient recovered. Rosenbaum wrote, "The case thus illustrates the high safety factor of the drug," and concludes "The mild toxic symptoms encountered are well compensated by the striking and gratifying anticonvulsant action of the drug in many cases."

Still another case of acute poisoning from Dilantin is recorded by Robinson.⁶² His patient took 45 gm. at one dose and recovered. Incidentally, a week later he was continued on Dilantin, 0.1 gm. three times daily, and "when seen six weeks later he showed no unusual sequelae."

It would seem that Dilantin Sodium has passed the experimental phase and found a definite place in the treatment of epilepsy, in spite of toxic symptoms. Its margin of safety as judged by acute poisoning appears to be considerable.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29131

PRESENTATION OF CASE

A fifty-nine-year-old Russian restaurant porter came to the hospital because of abdominal fullness, anorexia and loss of weight.

The patient apparently was well until two months before entry, when he developed constipation, which was relieved by saline purgatives. Occasionally his stools were black, but at no time were they bloody or acholic. Six weeks before admission, his appetite began to fail and his diet consisted largely of soups, cake, milk and fruit. One week later he began to suffer with a "burning feeling" in the upper abdomen, which was associated with frequent belching and was unrelated to meals or any particular food. Soon after this his urine became "brown, like tea" and he developed nocturia (ten or twelve times). Occasionally, in the morning he had shaking chills, which were followed by drenching sweats. About the same time he noted a nontender mass in the upper abdomen. Ten days before entry his ankles became swollen. There was no diarrhea, vomiting, jaundice, dyspnea, orthopnea, anginal pain, palpitation, flank pain, hesitancy, dribbling, dysuria or hematuria. He had lost 40 pounds of weight during the year previous to admission.

The family history was noncontributory. The patient was born in Russia but had lived in Massachusetts for forty-two years. He had worked in an iron foundry and a cloth mill, and more recently had been a porter in a restaurant. His diet was said to have been good prior to the present illness. Since the age of twenty-one he drank one or two glassfuls of beer or jiggers of whiskey daily, but he had had neither during the six months prior to admission. He denied having had rheumatic, typhoid or typhus fever or malaria.

Physical examination disclosed a pale, wasted man who was slightly dyspneic on exertion. The chest was barrel shaped and hyper-resonant. The examination of the heart and lungs was negative. The abdomen was markedly protuberant and the skin seemed tense. In the upper abdomen there was a firm, smooth, nontender mass extending to the umbilicus. The mass moved with respirations

and seemed to be a part of the liver. The spleen was easily palpable and seemed extremely large. No ankle edema was demonstrated.

The blood pressure was 95 systolic, 40 diastolic. The temperature was 97.9°F., the pulse 65, and the respirations 20.

The examination of the blood revealed a red-cell count of 3,160,000 with a hemoglobin of 55 per cent and a white-cell count of 6800 with 68 per cent polymorphonuclear leukocytes, 28 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The urine was acid in reaction. On three occasions it showed a + or ++ test for albumin; the test was negative in nine examinations. In three examinations of a total of twelve, the urine was slightly positive for bile. The sediment occasionally contained a small number of white cells. The stool was guaiac positive once in seven examinations. The blood Hinton test was negative. The serum protein was 5.1 gm., the albumin 2.3 gm., the globulin 2.8 gm., and the nonprotein nitrogen 28 mg. per 100 cc.; the bicarbonate was 22.5 milliequiv., and the chloride 99.3 milliequiv. per liter. The cephalin flocculation test was negative. The prothrombin time was 33 seconds (normal, 20 seconds). A Congo red test showed 33 per cent retention of the dye in the serum; 2.12 gm. of hippuric acid was excreted in the urine in four hours (5.9 gm. of sodium benzoate was administered by mouth). An intradermal skin test with echinococcal antigen was negative. An electrocardiogram was not remarkable.

A flat film of the abdomen showed a small liver and an enlarged spleen. There was a single round opaque shadow in the right upper quadrant outside the kidney shadow that suggested a gallstone. The kidneys seemed normal in the intravenous pyelograms. In a chest roentgenogram the right costophrenic angle was obliterated, probably by adhesions. The lung fields were not remarkable. No esophageal varices were seen after a barium meal. The stomach appeared normal. A large mass lay above the stomach and could be separated from it. The mucosal markings of the stomach were normal, as was the duodenal loop. A barium enema showed that the transverse colon was depressed by a large midline mass; no other abnormality was demonstrated. Films of the long bones and pelvis and a lateral view of the skull showed no evidence of disease.

The patient did not respond to a high-vitamin, high-carbohydrate and low-fat diet, and the blood prothrombin time remained prolonged in spite of large doses of parenterally administered vitamin K.

A peritoneoscopy was performed on the eighth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: We are confronted with a patient who showed definite evidence of impaired liver function and a large upper abdominal mass. In the first place I shall review the evidence for failure of liver function.

The total protein was somewhat low and the globulin was greater than the albumin. That may be evidence of liver failure. The hippuric acid test was on the low side, definitely below what is usually accepted as normal.

Let us consider the prothrombin time, which I think is helpful in intrinsic liver disease. It was definitely prolonged and remained so in spite of what we may presume was adequate parenteral dosage of vitamin K. I think that is definite evidence of intrinsic liver disease—liver failure. There is some question of the absence of bile in the stool from the story, but if the increased prothrombin time was due to lack of bile salts it should have responded to vitamin K therapy. The anemia is consistent with liver failure but not specific for it. It is curious that, although they did a cephalin flocculation test, which was negative, there was no attempt to measure the blood bilirubin, which might be of some help. We can assume there was increase in blood bilirubin if the urine test was positive for bile. I assume that it was, since it is so stated, definitely, on three occasions. I think I may be getting more fussy as the years roll by, but I spend a lot of time talking to the second-year students on the value of looking at a stool, and in this case I should rather know what it looked like than to know it was guaiac positive. It is fair to assume, it was normal in color. Thus, there is evidence of impaired function of the liver—evidence that is consistent with cirrhosis of the liver.

Against the diagnosis of cirrhosis of the liver are the absence of esophageal varices, the negative cephalin flocculation test—if you believe in it—and a clinical course that seems more rapid than that in the ordinary type of cirrhosis of the liver.

Let us turn to the abdominal mass. Clinically it was in the upper abdomen, in the midline, moved with respiration, and was thought to be attached to the liver. By x-ray the mass was said to have been above the stomach; whether that means cephalad or anterior, I do not know.

DR. GEORGE W. HOLMES: It means cephalad.

DR. RICHARDSON: And if it displaced the transverse colon, it probably displaced the stomach too. Perhaps we might look at the plates.

DR. HOLMES: In the chest film the lung fields are negative except for this obliteration of the angle between the diaphragm and the chest wall, low down on the right; I should say that it is neg-

ative for anything that has any bearing on the symptomatology in this case. The heart is somewhat enlarged, and the vessels perhaps a little prominent. What could produce such an appearance as that? Of course, an inflammatory process, either just above or below the diaphragm might result in such an appearance, or it could be in some way connected with this mass, which we see below the diaphragm on the left side. In the oblique view the angle between the chest wall and diaphragm is obliterated in front. I do not believe that is of importance. In this film you see the mass that has been described.

DR. RICHARDSON: On which side.

DR. HOLMES: On the left side. This is the case.

DR. RICHARDSON: And this shadow was thought to be spleen?

DR. HOLMES: Yes; enlarged spleen, I suppose.

There is a pressure defect in the upper portion of the stomach. The kidneys were studied in an attempt to rule them out as part of the mass; I should say that they are normal. The outline of the liver is indefinite, but the organ is small rather than large. The fact that these films do not show varices does not prove that they were not there; even with a careful examination they are sometimes missed.

DR. RICHARDSON: Does the gallstone show here?

DR. HOLMES: I do not see it.

DR. RICHARDSON: What was the mass? I do not believe it was due to an infectious process. There is a history of fever before entry to the hospital, with chills and drenching sweats, but it does not appear to have been prominent during his stay in the hospital. The blood picture is against a pyogenic infection, but of course it is consistent with some other type of infection. Nor do I see any good reason for talking about such things as echinococcal cyst, which usually has a much longer course than this and does not result in such serious symptoms so quickly.

I do not see any good reason to doubt that this was some type of tumor. A tumor in this region that produces this degree of displacement is difficult for me to explain unless it actually involves the liver. I cannot conceive of its being pancreas. It was said to move with respiration. One can consider various types of cysts and so forth, but the whole impression is that of a rapidly progressive disease. I asked about the gallstone because of the question whether one should consider biliary-tract carcinoma superimposed on an old chronically inflamed gall bladder with stones, and I think one should have that in mind. My impression is that this is a tumor. If it is a tumor, and if it involves the liver, we have no evidence of

its primary source. Having built up a case that is consistent with intrinsic liver disease—and I might say parenthetically that such a condition could explain the enlargement of the spleen—on the basis of a cirrhotic liver, one is justified in considering a diagnosis of primary liver tumor or hepatoma. The only difficulty with this diagnosis is that the tumor seems to have extended far down in the abdomen. However, it might have been on the under surface of the left lobe. I still think it was a liver tumor.

I conclude that the patient had underlying liver failure, probably portal cirrhosis of the liver, and that there was a tumor in the abdomen, probably a primary tumor of the liver, otherwise known as hepatoma.

In every case that one sees in medicine there is some mystery. The mystery in this case is, Why did anyone do a Congo red test? It was done, and if I interpret these findings correctly it was positive according to the criteria of some observers; 67 per cent of the dye was removed from the serum, which I think some members of the Arthritic Service would say was definite evidence of amyloid disease. My experience on the Medical Service is that amyloid disease is extremely rare. I cannot see how to fit it into this problem. I do not recognize a condition of localized amyloidosis that would cause a local tumor limited to the liver.

Another thing that bothered me is that the person who abstracted this record made a great effort to make it clear that there was no real evidence of nephrosis in the urine. There was albumin on only one or two occasions, and the suggestion seems to be that there should have been more albumin. However, in spite of all the things about amyloid disease, I do not believe that one can count on a Congo red test to make a diagnosis. This patient did not have amyloidosis, either from the clinical picture or from the physical or x-ray findings. If it was present I am sure it was purely incidental.

There is one further point in regard to the anemia: it could have been due to cirrhosis of the liver, but it also could have been due merely to malnutrition and lack of some of the factors necessary for blood formation.

My final diagnoses are portal cirrhosis of the liver and primary tumor of the liver.

DR. CHESTER M. JONES: I suggest that Dr. Holmes be asked whether the left lobe of the liver was enlarged, even though it looks small, and the x-ray report stated that there was a "small liver." With the displacement of the stomach it looks as if the left lobe might have been large.

DR. HOLMES: I agree that there is a mass in the region of the left lobe of the liver; whether it

is an unusually shaped liver or a tumor, I do not know.

DR. J. H. MEANS: This case puzzled us enormously, and I should like to congratulate Dr. Richardson on his excellent handling of it. The abstract oversimplifies the situation by including the x-ray findings and not the peritoneoscopic findings, which were at variance. The radiologists thought the liver was small, and the endoscopist thought it was large. I think we should have been a great deal better off if we had not had so much expert advice.

We knew the patient had a "sick liver." That was obvious enough, but we thought he must have something else, just as Dr. Richardson did. What I felt in the abdomen was rather odd. I made out a huge organ with an edge. Whether it was liver or liver plus spleen, I was not certain. The outline was rather queer for liver. It went in the wrong direction on the right side. In other words, it went from northwest to southeast, and then made an angle and went up in a northeasterly direction from below the umbilicus. I was gratified that the autopsy findings disclosed that that was a fairly correct description of what was present.

I am rising to the defense of the Congo red test—I asked for it. There are several points in common between this case and that of a colored girl we had seen eight months earlier. She had a huge liver and spleen and ran a fever very much like this man's. We did a Congo red test and found that she took up all the dye. It was positive on two occasions. Then we got Dr. Benedict to look in. We hoped that he would find some organ stained red with the dye, but he could not do so. Because the cases had points of similarity I thought it would be interesting to do a Congo red test on this man. He had a positive one, but I do not know how to interpret it. That is as far as we got. We treated him for the sick liver, which we knew he had. He was reluctant to let us give intravenous injections and finally rebelled completely, when he went steadily downhill and died.

Should we not hear from the endoscopist?

DR. EDWIN B. BENEDICT: There was no tumor. The liver and the spleen were enlarged—two separate masses, with fluid in the abdomen. Also, I should like to rise to the defense of the endoscopist, because I think his findings proved to be more accurate than those of the radiologist.

CLINICAL DIAGNOSIS

Lymphoma, with metastases to spleen?
Gaucher's disease??

DR. RICHARDSON'S DIAGNOSES

Portal cirrhosis of liver.
Primary tumor of liver (hepatoma).

ANATOMICAL DIAGNOSES

Subacute hepatitis, with diffuse cirrhosis (? syphilitic).

Ascites.

Splenomegaly, slight.

Cholecystitis, chronic.

Cholelithiasis.

Arteriosclerosis, moderate.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: As I read over this history I made the same diagnosis as Dr. Richardson did, which is wrong. I am not quite so sure what the correct diagnosis is.

The liver weighed 2300 gm. The enlargement, however, was almost entirely in the left lobe, the right lobe having shrunk. As a result the liver had pivoted on its suspensory ligament, and its edge ran diagonally across the abdomen in the wrong direction, as Dr. Means has described in mariner's terms. The spleen was moderately enlarged. There were some questionable varices in the esophagus, which were not extremely impressive. No tumor was found. The mass was the hypertrophied left lobe of the liver. The organ as a whole was very finely granular, and except for the disproportion of size, the two lobes were similar.

On microscopic examination it shows an extremely diffuse fibrosis, which not merely encapsulates lobules and nodules of liver tissue but invades every lobule. The distribution of fibrous tissue is much like that of amyloid deposits in the liver; the liver tissue, however, failed to give a positive amyloid reaction. There also is an active progressive hepatitis, with monocytes and lymphocytes predominating in the infiltrate. If I saw this microscopic picture in a child I should have no hesitancy in saying it was congenital syphilis of the diffuse type. Most textbooks of pathology say that diffuse syphilis of the liver, though extremely rare, may occur in an adult. Dr. Alexander J. Michie reminded me of McCrae's* paper on syphilis of the liver. That is a purely clinical study, but this case fits well and the fever is characteristic. Involvement of the left lobe has apparently been noted in more than half the cases. Negative serologic tests are said to be not extremely unusual, although, of course, McCrae's paper was written before the days of precipitation tests, when one had to rely exclusively on the Wassermann test. The demonstration of spirochetes could settle the diagnosis, but our efforts to date have proved fruitless.

DR. JACOB LERMAN: On rounds we discussed the possibility of the left-lobe enlargement's being due

to syphilis, but we placed a lot of emphasis on the negative Hinton test and therefore ruled it out.

DR. MALLORY: It is too bad that we did not repeat the serologic test using dilutions of the serum. The serum from a patient of this sort might have such an extremely high titer that it would give a prezone phenomenon.

DR. RICHARDSON: What happened to the red dye?

DR. MALLORY: We found none of it.

CASE 29132

PRESENTATION OF CASE

A twenty-seven-year-old married dentist was referred to the hospital because of fever and a persistent nonproductive cough of six weeks' duration.

The patient had always been in excellent health until three months before admission when during the summer, without known precipitating factors, he experienced a sharp pain that began in the right shoulder but soon settled in the anterior right chest. This was made worse by deep respirations and movements of the trunk. Six weeks before admission he suddenly developed a nonproductive irritating cough but did not have an upper respiratory infection. This continued to the day of admission without any change in severity and did not respond to cough medicine prescribed by his physician. Two weeks before entry the physician found that the patient's temperature was 100.2°F., the pulse 120, and the respirations 30. Chest films at another Boston hospital were said to have revealed "a mass in the right lung that was cystic and contained fluid." During the week prior to admission he had a daily temperature elevation to 101°F. and drenching night sweats. There was no hemoptysis, weight loss, palpitation, dyspnea, chills or cyanosis.

The family history was noncontributory. The patient was born in Boston and had lived there most of his life.

Physical examination disclosed a well-developed and well-nourished man in no apparent distress. The trachea was in the midline; the chest seemed symmetrical, but there was some lag in expansion on the right. There were dullness and diminished breath sounds on the right side to the level of the eighth rib posteriorly and the clavicle anteriorly. Scattered crackling rales and bronchovesicular breathing were audible in the midscapular region. Examination of the left lung, heart and abdomen was normal. There was minimal clubbing of the fingers.

The blood pressure was 130 systolic, 82 diastolic. The temperature was 98.6°F., the pulse 123, and

*McCrae, T., and Caven, W. R. Tertiary syphilis of liver. *Am. J. M. Sc.* 172:781-796, 1926.

the respirations 35. The pulse and respirations remained rapid throughout hospitalization. The temperature rose to 100.4°F. on the fourth hospital day and subsequently varied between normal and 102°, but did not rise in abrupt sharp peaks.

The hemoglobin was 12 gm. per 100 cc., and the white-cell count 16,900. The urine was acid in reaction and had a specific gravity of 1.020; the sediment contained rare red and white cells. The blood Hinton test was negative.

A chest roentgenogram disclosed a 12 by 15 cm. smooth, homogeneous mass that filled the anterior two thirds of the lower right chest and rose to the level of the second rib anteriorly. The mass appeared to arise from the anterior mediastinum on the right side. The right main bronchus and its subdivisions were not grossly abnormal. There was a small amount of fluid in the right pleural space. The left lung field was clear; the heart was not definitely abnormal and the left diaphragmatic shadow appeared normal. There was no evidence of mediastinal shift or of definite esophageal displacement.

An operation was performed on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN BRUES: I have culled briefly the significant points in this short report. We have a twenty-seven-year-old dentist who, for three months, had anterior chest pain heralded in by shoulder pain, pleural in type, which was increased by respirations and by movements of the trunk. Six weeks before entry he developed a cough, which apparently was never productive. Four weeks later, fever was first noted, which was of a mildly septic type. After that he had tachycardia and rapid breathing, but no general prostration. There was a mild anemia, and a minimal clubbing of the fingers; physical and x-ray examinations agree in the mass in the right anterior chest coalescent with the mediastinum, with a small amount of pleural fluid on that side. There are also two collateral observations that I should like to bring up. First the outside x-ray films which, using legal terminology, we might call "hearsay evidence," which may be important. The description given us is that of a cyst containing some fluid, and we should suspect that such a definite description would have been made only if a fluid level had been observed. We therefore have hearsay evidence that, at that time, instead of a solid lesion there was one which was thought to contain fluid and perhaps had a fluid level. The second collateral observation we may class in accordance with our legal analogy as "circumstantial evidence": an operation was performed. The operation must have

revealed something of sufficient significance to the Pathology Department to make it the subject of a clinicopathological conference. In other words, something more than pus must have been found.

One bit of evidence that is lacking is a blood smear. Perhaps it was not made. It might encourage or discourage certain diagnoses that I think for other reasons are improbable—namely, tuberculosis, in which the granulocytes are relatively low and the monocytes high; parasitic disease, which is usually accompanied by an eosinophilia; Hodgkin's disease, which often shows a high granulocyte count and possibly eosinophilia; and leukemia, in which a smear may give obvious evidence of the condition.

DR. TRACY B. MALLORY: The white-cell count was 12,400, with 79 polymorphonuclear leukocytes, 11 small lymphocytes, 8 monocytes and 2 eosinophils. The red cells and platelets appeared normal.

DR. BRUES: We have a process limited to the right chest with initial pain suggesting pleural involvement. I do not believe there was massive pleural involvement, such as we might expect with an endothelioma of the pleura, because of the small amount of fluid that is reported. We do however expect to find something encroaching on the pleura and giving the first symptom in that way.

I should like next to consider fever as a symptom. This suggests primary infection, some lesion secondarily infected or a series of other conditions that might be febrile, such as Hodgkin's disease, sarcoid and metastatic disease; of the latter, Ewing's tumor is the only commonly febrile representative and is out of the question without evidence of a primary lesion. I shall pass over sarcoid, and say in connection with Hodgkin's disease that the reported nonlobulated configuration of the growth, the fact that pain was the first symptom and occurred long before the others, and the fact, if true, that a fluid level was seen are against the diagnosis. Furthermore, fever in Hodgkin's disease is usually observed either in advanced cases or in cases with posterior rather than anterior mediastinal involvement.

It might be appropriate to take up the x-ray films at this point.

DR. GEORGE W. HOLMES: The films that I have put up cover a period of about three months. They show a very large mass that occupies the midchest. In the anteroposterior view it is in the central portion of the chest. In the lateral view it also appears to be in the midportion rather than in the front or back. It is of some interest that a mass as large as that does not displace the heart. We might assume that the lung was collapsed behind it, so that we do not see it, and that one compensates the other and there is no displacement. There

is evidence in this film of a small amount of fluid in the pleural space. The mass is homogeneous, with sharply defined borders, and is not lobular.

DR. BRUES: Does this exhibit include the plate taken in the outside hospital on which I was speculating?

DR. HOLMES: No. Of course that would be of great value.

In the spine the fifth lumbar vertebra has a narrow posterior portion. I do not believe that this represents metastatic malignancy.

DR. BRUES: We must still consider primary infections and secondarily infected processes. I shall first mention the possible primary infections. There was no history of pneumonia, and the x-ray films do not suggest that the lesion was of that type. The course was not septic enough to suggest a large encapsulated empyema, and I suspect that the rounded lower border of the mass by x-ray makes an interlobar accumulation of fluid or pus unlikely.

Tuberculosis, of course, is suggested by the first few lines in the record. The significant point against tuberculosis is the absence of disease in the apices. One might also think of two other processes similar to tuberculosis but without the same tendency to occur in the apices—actinomycosis and streptothricosis. Either of these, however, should give greater prostration.

An amebic abscess working its way up from the liver is indicated in the beginning of the history since the pain occurred in the shoulder, suggesting something in the region of the diaphragm. One might think of an amebic process passing from the liver through the diaphragm, settling in the lung and giving these symptoms. Again, one would expect considerable prostration.

Against echinococcal disease is the fact that the patient was apparently a confirmed Bostonian.

Did he have a lung abscess? Such a process would have been walled off rather thoroughly, since there was no sputum, which is strongly against the diagnosis. Furthermore, the x-ray films show no particularly marked degree of infiltration around the process.

The fact that the fever occurred late suggests a secondary process. Cancer of the lung, centrally located, can be walled off so that no sputum appears, but this is unusual. The patient was young for cancer to occur, but not too young. In its favor is the lack of displacement of the mediastinum, such as may occur in an infiltrative lesion. Against it, for the same reason, is the absence of infiltration in other directions.

Two other processes start early in life and give their peak incidences of trouble in the third decade, namely, congenital cystic disease and dermoid cyst. Both of these may show a fluid level at some time.

Dermoids are particularly likely to occur in the anterior part of the chest coalescing with the mediastinal shadow and appearing low in the lung fields. One would expect a dermoid to displace the mediastinum to the opposite side, and that worried me somewhat, but I was inclined to pass that off, and Dr. Holmes has given me assistance in doing so. Therefore, because of the age, the location, the recent febrile course, the absence of sputum and the lack of definite evidence against it, I shall make the diagnosis of dermoid cyst, secondarily infected.

DR. MALLORY: What was the line of argument before operation, Dr. Brown?

DR. ROBERT K. BROWN: We thought the lesion probably was a dermoid cyst. The patient was extremely sick when he came in. His pulse is recorded at 120, but it ranged from 120 to 140 and did not go down after a week's rest in bed. The temperature went up and ranged from 100 to 102°F., not a definite septic temperature. Dr. Churchill thought that the patient was not in condition for open thoracotomy such as would be required in an attempt to remove the whole lesion, and decided merely to explore under local anesthesia through an anterior incision.

DR. MALLORY: I think you might as well go ahead and tell the operative findings.

DR. HOLMES: May I say a word first? If you arrive at a diagnosis of cyst there are some points in the x-ray examination that may help to decide between dermoid and other forms of cyst. For instance, an echinococcal cyst usually has calcified walls, and a dermoid cyst often shows variations in density within the cyst itself, such as teeth and areas of markedly diminished density due to fat. Although the latter may also look just like this one, the absence of variations in density is perhaps against it.

DR. RICHARD SWEET: I have just taken a dermoid cyst out of a mediastinum that showed marked calcification in the wall.

CLINICAL DIAGNOSIS

Dermoid cyst.

DR. BRUES'S DIAGNOSIS

Dermoid cyst, secondarily infected.

ANATOMICAL DIAGNOSES

Teratoma of mediastinum, with extension to middle lobe of right lung and metastases to liver and vertebrae.

Pathologic fracture of fifth lumbar vertebra.

Collapse of right lung, massive.

Bronchopneumonia, slight, of left lung.

Ascites.

Operative wound; exploratory thoracotomy.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Will you tell us the operative findings, Dr. Brown?

DR. BROWN: A large mass was found with a solid wall about 1 cm. thick and a necrotic center consisting of gray mushy material.

DR. MALLORY: A biopsy specimen showed a tumor which in part appeared to be carcinomatous with some rather poorly formed glands, which were enough to justify one in thinking of it as adenocarcinoma. Other portions of the tumor were composed of long spindle cells that looked fibroblastic. We thought we were probably justified in assuming that there were two kinds of cells and that this was therefore an undifferentiated teratoma rather than a carcinoma. Following that, x-ray treatment was given. Dr. Brown will tell the rest of the story.

DR. BROWN: The lesion did not change with 1,000,000-volt x-ray therapy, even in large dosage. In two months he came in again with a pathologic fracture of the fifth lumbar vertebra, which was treated by x-ray; the patient was put in a plaster shell. Two months later he came back terminally, with a large liver and ascites; he died in six days.

DR. MALLORY: At post-mortem examination we found a large tumor in the anterior mediastinum projecting into the pleural cavity. It was very firm and was adherent to the middle lobe of the right lung, and on section it was possible to show

that it had invaded the middle lobe. That left two possibilities—it was either a mediastinal teratoma with secondary invasion of the lungs or a primary carcinoma of the lung spreading into the mediastinum. It seemed to us from gross examination that the latter was unlikely since the tumor was largely at the periphery of the lung and the bronchi were entirely uninvolved, carcinoma of the lung with negative bronchi being, of course, a rarity. Coupling that with the peculiar histologic character we felt justified in continuing to call this a teratoma. There were extensive metastases to the liver and bone marrow, and the fifth lumbar vertebra was involved; there was nothing else of interest. The tumor was perfectly solid at the time of autopsy and nothing suggested at that time that it had ever been cystic. I am not quite clear from the surgical report whether it was cystic at the time of operation. The center was soft, but no fluid or air was reported.

DR. HOLMES: Were there any signs of x-ray treatment?

DR. MALLORY: The tumor was almost totally necrotic. We could hardly find a viable cell in the mediastinal tumor in contrast to the liver, where the histology was essentially that of the biopsy specimen.

DR. HOLMES: I suppose that the change in the fifth lumbar vertebra does represent a metastasis. However, it is wedge shaped, the reverse of what it should be with a pathologic fracture.

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BACK TO THE LAND

WHEN the conflict is over and the olive branch has blossomed and borne fruit, then, traditionally, the swords of the armies are beaten into ploughshares and their spears into pruning hooks. Or so said the Lord speaking through the tongues of Isaiah and of Micah. This, however, is only the second half of the allegory. It had first been necessary to beat certain ploughshares and pruning hooks into the swords and spears, and to place on priority lists the materials from which they had both been made.

It is implicit in the nature of democracy that when an aroused but unprepared and normally

peace-loving people go to war they have to abandon their ploughs in the furrows (even before they are beaten into weapons). They never realize at the time that these implements are mighty weapons in their own right. Thus, at least, did Cincinnatus, and probably many a patriot, like the minuteman arrested in bronze beside the Concord River, in the midst of the ploughing season of 1775. Who planted the crops in those stirring days and later harvested them is left to the imagination, and our present predicament offers no satisfactory explanation. We may assume, however, that not all the machinery of agriculture was left to rust in the fields,—although that bucolic custom also has continued to the present day,—but that the women and boys and grown girls, being fit for the kingdom of God, did not look back, having put their hands to the plough. By some similar arrangement we must manage to get our own crops sown and harvested today.

With many of the commercial farmers failing us this year owing to the shortage of farm labor, it is necessary that a good deal of amateur gardening be undertaken, not all of it with benefit of press photography, and some of it resisting stubbornly the classification of "victory gardening." A considerable power of vernal enthusiasm is going to wilt under the summer sun, and since a great quantity of seed will be planted it is probable that more than the usual proportion will fall by the wayside or upon stony places or among thorns. Much of this crop will stand us in good stead, but it will be a wasteful crop, and better organization is going to be necessary if we are to keep potatoes in the barrel next winter.

The boys and girls of high-school age constitute the logical group to enlist for this particular, important effort, and so far as possible their task forces, adequately supervised, as their social activities should be adequately chaperoned, can be mobilized where they are most needed. This should include as little as possible in amateur victory gardening, praiseworthy as that effort is, and as much as possible in substantial farming, under the direction of capable farmers.

We are inclined to initiate anything with a burst of enthusiasm and often with a good many preliminary mistakes. A certain number of youngsters will be (and have been) put on farms where they will be more of a nuisance to the farmer than they will be a help. Some farmers view this back-to-the-farm movement with more concern than that with which they witnessed the on-to-the-city trek of earlier decades. Vacation help is limited, also, to only part of the farming season; it is available too late for planting and departs too early for the late harvest. It serves, nevertheless, two valuable purposes: it furnishes healthful summer vacations for the workers, and it makes a real and urgent contribution to the national effort.

The movement is under way; it has functioned quite satisfactorily already. Work camps have been successfully conducted, and many of the private summer camps are now adding farming to their activities. There is plenty of land on which to grow all the crops the world needs, but brains, organization and unceasing effort are required to keep it in production.

INVALID DIETS AND FOOD RATIONING

RATION ORDER 13, issued by the office of Price Administration under the date of February 9, 1943, is of interest to all who are concerned with diets for invalids. The order covers all canned, dried and frozen fruits and vegetables, and Article II, Section 2.5, reads as follows:

Consumers who need more processed foods because of illness may apply for more points:

(a) Any consumer whose health requires that he have more processed foods than he can get with War Ration Book No. 2, may apply for additional points. The application must be made on OPA Form R-315 by the consumer himself or by someone acting for him, and may be made in person or by mail. The application can be made only to the board for the place where the consumer lives. He must submit with his application a written statement of a licensed or registered physician or surgeon, showing why he must have more processed foods, the amounts and types he needs during the next two months, and why he cannot use unrationed foods instead.

(b) If the board finds that his health depends on his getting more processed foods, and that he cannot use or cannot get unrationed foods, it shall issue to him one or more certificates for the number of points necessary to get the additional processed foods he needs during the next two months.

Form R-315 is likely to be confusing to patients, since it is titled "Sugar Special Purpose Application," having been developed to meet the demand for extra sugar for home canning. It is being used temporarily until a more adequate form is available.

This method of obtaining additional rationed foods will probably be modified in the future; if so, due notice of any change will be provided.

MEDICAL EPONYM

TAY-SACHS'S DISEASE

Warren Tay (1843-1927) reported "Symmetrical Changes in the Region of the Yellow Spot in Each Eye of an Infant" (*Tr. Ophth. Soc. U. Kingdom*, 1:55-57, 1881). He writes:

Mrs. L.—brought her infant, aet. 12 months, to the London Hospital, March 7th, 1881. When the baby was a fortnight or three weeks old, it was noticed to have very little power of holding its head up or of moving its limbs. Since that time the weakness had become more and more pronounced. . . . It seemed to me that its cerebral development was probably deficient, and I was induced to examine the eyes with the ophthalmoscope to ascertain whether there was any affection of the optic nerves. . . . I found the optic discs apparently quite healthy, but in the region of the yellow spot in each eye there was a conspicuous, tolerably defined, large white patch, more or less circular in outline, and showing at its centre a brownish-red, fairly circular spot, contrasting strongly with the white patch surrounding it.

Bernard Sachs (b. 1858) read a paper before the American Neurological Association in July, 1887, entitled "On Arrested Cerebral Development, with Special Reference to its Cortical Pathology" (*J. Nerv. & Ment. Dis.* 14:541-553, 1887). A portion of the article follows:

The little girl S., who was but two years old at time of death, was the first-born of young and healthy parents. . . . Nothing abnormal was noticed until the age of two to three months, when the parents observed that the child was much more listless than children of that age are apt to be; that it took no notice of anything, and that its eyes rolled about curiously (there was evident nystagmus). Allowing for

some very slight vacillations, the child remained in practically the same condition up to the time of death.

The child as it grew older gave no signs of increasing mental vigor. It could not be made to play with any toy, did not recognize people's voices and showed no preference for any person around it. During the first year of its life, the child was attracted by the light, and would move its eyes, following objects drawn across its field of vision, but later on absolute blindness set in.

Dr Knapp, who made several ophthalmoscopic examinations of this case, reported the following unusual condition: Child two to three months, nystagmus vibratilis, pupils contracted as is usual with children at this age. Media clear, optic nerve visible. Fovea centralis, of a cherry red color was surrounded by an intense grayish white opacity. This opacity was most distinct in the vicinity of the fovea centralis, and for some little distance around it but faded away gradually into normal retinal field. "a further examination in May and June, 1886 revealed great changes. Child totally blind, optic nerves completely atrophied (disks as white as paper, with scarcely a trace of blood vessels). Macula lutea essentially as before".

During last summer (1886), the child grew steadily weaker, it ceased to take its food properly, its bronchial troubles increased, and finally, pneumonia setting in, it died August, 1886.

R W B

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON INDUSTRIAL HEALTH

The Committee on Industrial Health will hold an all-day meeting at the Harvard Club of Boston on Saturday, April 24. Except for the omission of the dinner in the evening, this meeting will be similar to that held at the same place last November, with an entirely new program. Among the subjects covered will be the following: the methods used in establishing diagnoses of industrial poisoning; the late effects of craniocerebral trauma; the medical aspects of absenteeism in industry; the present status of the relation of heart disease to industry; epidemic keratoconjunctivitis; and the problems of women in industry. There will also be a panel discussion of the surgical, medical, insurance and preventive aspects of diabetes in industry. Other subjects will be added, and all papers will be delivered by recognized experts in their various fields. The program will start at 9.30 a.m. and should be concluded by 5.00 p.m.

Parking facilities will be available in the rear of the Club, on Newbury Street. There will be a registration fee of 50 cents to cover the cost of arrangements, and luncheon (\$1.50 per plate) will be provided for those who make reservations. The facilities of the Harvard Club will be at the dis-

posal of those in attendance, thus ensuring a comfortable and sociable atmosphere for all. Physicians, as well as personnel managers, nurses and others interested in safeguarding the health of workers in industry, are cordially invited to attend, and may register by addressing the Committee on Industrial Health, at 8 Fenway, Boston. Owing to wartime conditions, reservations for luncheons must be made at least forty-eight hours in advance.

All physicians who are interested in industrial health are assured a pleasant and profitable April 24. They should mark the date on their calendars and send their checks for \$2.00, covering registration and luncheon, to the committee before April 22.

DWIGHT O'HARA, *Chairman*

WAR ACTIVITIES

INDUSTRIAL MEDICINE

MEDICAL CARE FOR SMALL INDUSTRIES

In New York City a group of small industries has been considering a plan to provide medical care for their workers on a co-operative basis. The plan was drawn at their request by Group Health Co-operative, Incorporated, a nonprofit medical insurance organization.

The problem in small plants has been one of dealing with unfamiliar industrial hazards, inexperience with industrial medical service, and lack of funds to supply needed medical service. A solution seems to be some outside agency with the necessary organization to provide a common service for a number of small plants in a given area on a co-operative basis.

The plan drawn up would supply in plant services through full time industrial physicians (one physician for each 2000 employees) and nurses (one for each 500 employees). These in plant services would include emergency treatment of accidents and illness while on the job, pre-employment and periodic physical examinations, medical check-ups on employees returning to work after absence, supervision of plant hygiene, and co-operation in safety programs and health education. The industrial physician would render only emergency treatment in compensation cases, and the patient would, under the laws of New York State, be free to choose his own physician for subsequent care.

Closely correlated with these in plant services is provision for home and office care and diagnostic specialist service for nonindustrial conditions, which constitute the major cause of absenteeism. The out-of-plant service would be rendered by a panel of doctors open to any licensed physician in the community. The employee would have completely free choice of any physician on the panel.

Because of objections raised by some employee groups to physical examinations conducted by industrial physicians, the plan provides alternately for pre-employment and periodic examinations to be rendered by the panel physician of the employee's choice.

It is hoped that close co-operation can be obtained between the in plant and outside services through the medium of the central organization. The family doctor and the industrial physician should not operate as two sepa-

rate units, but as equal guardians of different phases of the employee's health.

It is intended that this service should be financed by the employer at a basic premium per employee of \$1.42 each month. For each home visit by the physician of his choice, the employee would incur a charge of \$1.00, payable directly to the physician.

In addition to this projected plan, Group Health Co-operative now has in operation a plan covering surgical, obstetrical and in-hospital medical care. This plan costs \$9.60 a year for an individual or \$24 for a family. The combination of these two plans would provide workers in war industries with comprehensive and integrated medical care at the plant, at home and in the hospital. — Reprinted from *Industrial Hygiene*, a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1942

DISEASES	DECEMBER 1942	DECEMBER 1941	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	2	7	3
Chicken pox	1444	1603	1512
Diphtheria	14	19	18
Dog bite	516	550	570
Dysentery, bacillary	6	16	16
German measles	190	68	14
Gonorrhea	286	273	359
Measles	1871	678	835
Meningitis, meningococcal	28	11	6
Meningitis, other forms	9	6	†
Mumps	1080	1460	634
Paratyphoid infection	7	4	3
Pneumonia, lobar	327	208	367
Scarlet fever	1312	1171	731
Syphilis	489	335	420
Tuberculosis, pulmonary	249	241	274
Tuberculosis, other forms	14	26	29
Typhoid fever	3	9	8
Undulant fever	2	3	5
Whooping cough	1171	828	801

*Based on figures for preceding five years

†Pfeiffer bacillus meningitis only; other form reportable previous to 1941.

Anterior poliomyelitis was reported from: Palmer, 1; Springfield, 1; total, 2.

Anthrax was reported from: Middleboro, 1; total, 1.

Diphtheria was reported from: Boston, 1; Fall River, 2; Lexington, 1; Lowell, 2; Medford, 2; Methuen, 1; Newton, 1; Peabody, 1; Somerville, 1; Taunton, 1; Waltham, 1; total, 14.

Dysentery, bacillary, was reported from: Beverly, 1; Cambridge, 1; Peabody, 1; Waltham, 3; total, 6.

Meningitis, meningococcal, was reported from: Barnstable, 1; Boston, 4; Braintree, 1; Cambridge, 1; Camp Edwards, 1; Chelsea, 1; Fort Banks, 1; Fort Devens, 2; Gardner, 1; Lexington, 2; Lowell, 2; Lynn, 2; Mansfield, 1; Medford, 1; Middleboro, 2; Pittsfield, 1; Saugus, 1; Taunton, 2; Waltham, 1; total, 28.

Meningitis, other forms, was reported from: Boston, 1; Brookline, 1; Chicopee, 2; Cohasset, 1; Hardwick, 1; Leominster, 1; Quincy, 1; Springfield, 1; total, 9.

Paratyphoid infection was reported from: Boston, 2; Everett, 1; Lowell, 1; Melrose, 1; Spencer, 1; West Boylston, 1; total, 7.

Septic sore throat was reported from: Boston, 3; Cambridge, 1; Colrain, 1; Dedham, 1; Leominster, 1; Quincy, 1; West Springfield, 1; Worcester, 1; total, 10.

Tetanus was reported from: Norfolk, 1; total, 1.

Trachoma was reported from: Boston, 1; Cambridge, 1; total, 2.

Trichinosis was reported from: Boston, 2; Everett, 2; total, 4.

Typhoid fever was reported from: Boston, 1; Easton, 1; Medford, 1; total, 3.

Undulant fever was reported from: Cambridge, 1; Gloucester, 1; total, 2.

The general pattern of communicable-disease incidence for December shows no striking changes over that of last month.

Scarlet fever, whooping cough, measles and mumps are showing a decided upward trend. The scarlet-fever figure is a little less than the five-year average; measles, more than twice the average; and whooping cough well over the average and the highest figure since 1937, although still far from showing a record high.

Meningococcal meningitis has been increasing in incidence for the last two years; it is now four times the five-year average.

Other diseases that exceeded their five-year averages are German measles, mumps and syphilis.

Typhoid fever, paratyphoid infection, diphtheria and undulant fever, on the other hand, remain at low level. This month's diphtheria figure (14 cases) is next to the lowest December record since 1906.

Other diseases that fell below their five-year records are bacillary dysentery, lobar pneumonia, pulmonary tuberculosis, tuberculosis (other forms), gonorrhea, chicken pox and dog bite.

BOOK REVIEW

The Blood Bank and the Technique and Therapeutics of Transfusions. By Robert A. Kilduffe, A.M., M.D., and Michael DeBakey, M.D., M.S. 8°, cloth, 558 pp., with 214 illustrations and 1 color plate. St. Louis: The C V Mosby Company, 1942. \$7.50.

Physicians in all branches of practice are using transfusions of blood, serum and plasma with increasing frequency. In war casualties the use of blood and its derivatives has been largely responsible for the salvage of the great numbers who would have died from shock thirty years ago.

The procedure of transfusion, simple as it is when properly done, is constantly fraught with dangers of a reaction. This work gives detailed consideration to the precautions that are necessary for the avoidance of such undesirable sequelae to transfusion.

With the advent of the blood bank, an entirely new factor has developed in the field of transfusion. It was to be hoped that stored blood would fill all the needs for fresh blood. But such is not the case, and in summarizing this aspect of the problem the authors say: "From the studies above discussed, it is apparent that although stored blood may be, and indeed has been shown conclusively to be, effectual in the treatment of shock and acute hemorrhage, it is definitely inferior to fresh blood in the transfusion treatment of acute and chronic infections, hemorrhagic states and the anemias. When stored blood is used in such conditions, the maximum storage period should preferably not exceed seventy-two hours."

Much of the text is devoted to the technics for transfusions, the operation of a blood bank and the preparation of blood derivatives, such as plasma and serum. These chapters have many illustrations to enable one easily to follow the methods described.

This is a timely book, and the authors have rendered great help to the people who must organize and run a transfusion service, whether in a large hospital or a fighting unit.

(Notice on page xi)

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THE DIAGNOSIS AND TREATMENT OF LUDWIG'S ANGINA*

A Report of Twenty Cases

ASHBEL C. WILLIAMS, M.D.,† and WALTER C. GURALNICK, D.M.D.‡

BOSTON

IN a recent communication, one of us (A.C.W.¹) presented a study of 31 cases of Ludwig's angina. In that study, an effort was made to ascertain the pitfalls most frequently encountered in the treatment of such patients and, with these hazards in mind, to set forth a plan of management calculated to give the highest degree of success. In a second paper² appearing somewhat later, suggestions were made pertaining to the choice of anesthetic in Ludwig's angina, it being clearly recognized that anesthesia constitutes a major problem, the successful solution of which is essential to an adequate surgical procedure. The present report consists of an analysis of 20 consecutive cases of Ludwig's angina, representing all the patients with this disease seen at the Boston City Hospital during the three years from June, 1939, to June, 1942. These cases comprise all those seen at the Boston City Hospital since the submission of the original report. Twelve of the patients were seen by us personally, and 8 were under the treatment of our colleagues, with whom we were closely associated. Thus considerable opportunity has been afforded us to test the validity of our previous conclusions and to expand our knowledge of this disease.

The mortality in the present series was 10 per cent, compared with 54 per cent in the earlier one. Such a clear-cut improvement offers tangible substantiation of the principles of treatment previously advocated, and warrants the reporting of our more recent experiences. Accordingly, this paper will be largely confined to the presentation of these experiences and the opinions derived therefrom.

DIAGNOSTIC CRITERIA

Inflammatory diseases in the submandibular region and about the floor of the mouth are com-

monly subject to diagnostic error. Ludwig's angina is no exception. The disease is either not recognized or is wrongly diagnosed as submental abscess, cervical adenitis, cellulitis of the submaxillary gland or some similar condition. The essential criteria are anatomical as well as clinical.

Anatomically, there must be inflammatory involvement of both the sublingual and submaxillary spaces. The former is recognized by edema, induration, tenderness and elevation of the floor of the mouth, the mucosa of which is usually flecked with a dirty grayish-white exudate. Also, the tongue usually shows varying degrees of edema, so extensive in some cases that it reaches several times its original size and fills the oral cavity, protruding anteriorly between the teeth (Fig. 1). Submaxillary-space involvement is manifested by a rounded, tense, brawny, tender swelling, maximum in the region of the submaxillary gland and limited chiefly to the suprahyoid region of the neck (Fig. 2). This swelling may be unilateral or may involve both sides, depending on the duration of the disease. Fluctuation is rare, having been noted in only 1 of the 31 cases of the previous series and in none of the 20 recent cases.

Clinically, the patient has difficulty with speech, and in extreme cases may be unable to talk. The same is true of swallowing. He may be able to open his mouth only slightly or not at all. Difficulty with breathing is the last complaint chronologically and is evidence that a most critical state has been reached. Patients may well die without ever having complained of respiratory embarrassment. Similarly, cyanosis is infrequent. Patients usually drool at the mouth because of inability to swallow their saliva. Mucus may accumulate in the trachea because the patient is unable to expel the secretions, the airway being narrowed by the swelling higher up.

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ETIOLOGY

In the previous report, the source of the infection appeared to be dental in 51 per cent of the cases. It was surprising to discover that some type



FIGURE 1. Case 7.

Swelling and protrusion of the tongue are particularly well shown in this photograph, obtained before operation. Typical submandibular swelling was also present, but is not obvious. Reproduced from Current Researches in Anesthesia and Analgesia² by courtesy of the publisher.

of dental lesion was apparently the initiating factor in 18 (90 per cent) of the present series. For this reason, the etiologic role of dental lesions in Ludwig's angina should be further publicized.

Dental extractions immediately preceded the onset of symptoms in 12 cases. In 6 other cases, definite dental complaints preceded the illness, but no extraction, filling or other dental procedure had been performed.

The histories in the cases in which dental extractions had been performed are quite similar. The following one is typical.

E. P. (Case 3), a 10-year-old girl, was admitted with typical signs and symptoms of Ludwig's angina. She had noted a toothache 1 week previously, and under novocain anesthesia two molar teeth had been extracted from the right lower jaw 3 days previously. The day after the

extraction, she experienced discomfort in swallowing. Swelling was noted in the right submaxillary region. Her dentist advised the application of an ice bag. Twenty-four hours later, the swelling had markedly increased, swallowing had become extremely painful, and the patient could open her mouth only slightly. On the 3rd day following the extraction, her condition was worse. A physician was called and advised immediate hospitalization.

Of equal interest and importance are the histories in those cases that were thought to be of dental etiology but in which no extraction had been performed. The following case is illustrative.

T. C. (Case 14), a 10-year old boy, was admitted with classic signs and symptoms of Ludwig's angina. His tongue was so swollen that it filled the mouth and protruded between the upper and lower teeth anteriorly.



FIGURE 2. Case 3.

Submandibular swelling is the most prominent sign displayed in this photograph, taken prior to operation. Edema of the tongue and elevation of the floor of the mouth, not visible in this picture, were nevertheless present and in a moderately advanced stage.

He could neither talk nor swallow and had difficulty in breathing when lying down. There was marked swelling of the submandibular region, especially on the left. He had begun to suffer from a severe toothache in the left lower jaw 4 days before entry. A day later, he complained of swelling of the left jaw and a sore throat. His condition became steadily worse. A physician saw him 4 days after the onset of toothache and advised immediate hospitalization. Operation was performed shortly after admission. Convalescence was satisfactory. Before the patient was discharged, x-ray examination showed that

carries had invaded the pulp of the left lower first molar tooth. The tooth was extracted, and the patient was discharged completely recovered.

Patients are prone to blame the dentist if Ludwig's angina develops following a tooth extraction. However, the act of extraction is not so important from the standpoint of etiology as is the pre-existing septic tooth or mouth from which the subsequent spread of infection arises. The dentist who is unfortunate enough to have performed an extraction on a patient who subsequently develops Ludwig's angina is more likely to have been incidental to the train of events than to have been the responsible agent. Furthermore, there is no doubt that dental extractions occasionally avert the development of Ludwig's angina by removing a dangerous potential source of origin while the infection is still localized.

Whatever may be the etiologic role of dental extractions, the dentist is in a position to do much to prevent the final development of Ludwig's angina. In the first place, it has been fairly well established that many serious post-extraction infections may be avoided by careful preoperative preparation of the mouth.³⁻⁵ In the Dental Clinic of the Boston City Hospital, it was formerly the custom to employ mouth rinses with a 1:2800 solution of Metaphen five minutes previous to extraction. During the past year this routine has been discontinued in favor of zinc peroxide powder, which, in watery suspension, is used as a preoperative mouth wash. If the mouth be extremely foul, it is wise to instruct the patient to apply zinc peroxide powder to his teeth and gums several times daily for several days prior to extraction, during which time the bacterial flora will be modified and the hygiene improved so as to make extraction much less dangerous. Meleney^{4, 5} deserves the credit for suggesting this routine. Results at the Boston City Hospital have been gratifying. It seems wise, in this connection, to employ zinc peroxide powder prophylactically in any elective extraction, even though the mouth may appear clean. Details of its use have recently been described by one of us (W. C. G.).

After extraction has been performed the dentist should be on the alert for signs of impending trouble. Complaints of difficulty in swallowing should be taken seriously. Swelling of the jaw accompanied by even slight induration and elevation of the floor of the mouth calls for effective therapeutic measures. Patients who present this complaint should not be told merely to return home and apply ice packs. Chemotherapy with one of the sulfonamide drugs would, no doubt, be curative in a large number of cases at this stage. The continued use of zinc peroxide is advocated as a post-extraction

measure. Early hospitalization should be resorted to if the signs and symptoms progress further.

In the 2 cases not of dental origin, the infections were apparently primary in the pharynx, whence they spread forward and downward to produce the syndrome of Ludwig's angina. These 2 patients had had sore throats prior to onset.

BACTERIOLOGY

Streptococci have long been known to predominate as the causative organisms in Ludwig's angina. The presence of other organisms that grow best anaerobically has been mentioned previously.¹ In 16 (80 per cent) of the 20 cases in this series, culture reports were available; streptococci were present in all. In 8 of these cases, Vincent's organisms (fusiform bacilli and spirilla) were demonstrated by smear, showing that they invade along with streptococci. Whether or not the microaerophilic streptococcus described by Meleney⁴ was present is not known, since our culture techniques were not suitable to its demonstration. However, the presence of both streptococci and Vincent's organisms in 50 per cent of the cases makes it clear that in many cases one is not dealing with a straightforward streptococcal infection, but is faced with a more potent and rapidly progressive process, the synergistic effects of which have been pointed out previously by Meleney.

These bacteriologic findings have a significant bearing on treatment. Since all cultures yielded streptococci, there is a clear cut indication for sulfonamide drugs during the entire critical period of the disease. The presence of Vincent's organisms explains the foul odor so often characterizing the pus obtained at operation, and accounts for the stinking, extensive slough of the deep tissues often found in advanced cases and always noted at autopsy. We think that chemotherapy alone cannot be relied on in these synergistic infections, but should be made secondary to early radical incision of the area. Such a procedure allows access of air to the infected tissues and makes possible their further oxygenation through the medium of zinc peroxide dressings, thus inhibiting the anaerobes and thereby robbing the infection of its sharpest virulence. Perhaps it is not generally appreciated that, although not absolute anaerobes, Vincent's organisms should be treated as such since they thrive and are most dangerous under anaerobic conditions.

Other organisms such as staphylococci, which are not infrequently cultured from these wounds, are incidental and not of primary importance. No special measures as a rule need be taken on their account.

TABLE 1. *Summary of Data in 20 Cases of Ludwig's Angina.*

CASE No.	AGE	SEX	INTER- VAL FROM ONSET TO OPERATION <i>days</i>	DENTAL HISTORY	SCTION- AMIDE THERAPY	PRE- LIMI- NARY EXPO- SURE OF TRACHEA	TRA- CHI- TOMY	OPERATION	ANESTHETIC	DRESSINGS	SECOND- ARY CLOSURE	HOS- PI- TAL- IZA- TION <i>days</i>	RESULT
1	19	F	2	Extraction of 5 lower teeth	Sulfa-thiazole	Yes	No	Bilateral	Local and Pentothal	Zinc peroxide	6 mo. later	18	Living
2	63	M	1	None	None	Yes	No	Right side	Local and Pentothal			1	Dead
3	10	F	3	Extraction of 2 lower molar teeth	Sulfa-thiazole	No	Yes	Bilateral	Local and Pentothal	Zinc peroxide	No	38	Living
4	15	F	2	Toothache in right lower jaw	Sulfanil-amide	Yes	No	Right side	Local and Pentothal	Chlorinate packs	No	30	Living
5	12	M	1	Extraction of lower molar tooth	Sulfanil-amide	No	No	Bilateral	Pentothal	Zinc peroxide	No	21	Living
6	19	M	4	Extraction of lower molar tooth	Sulfa-thiazole	No	Yes	Bilateral	Local and Pentothal	Boric solution	No	5	Dead
7	21	F	5	Extraction of lower molar tooth	Sulfanil-amide	Yes	No	Bilateral*	Local and Pentothal	Zinc peroxide	No	18	Living
8	38	M	7	Swelling of gums, right molar region	None	Yes	Yes	Bilateral	Pentothal	Zinc peroxide	No	11	Living
9	22	F	5	Toothache in lower jaw	None	Yes	No	Left side	Local and Pentothal	Hydrogen peroxide	No	9	Living
10	22	F	3	Extraction of lower pre-molar tooth	Sulfa-thiazole	Yes	No	Left side	Local and Pentothal	Zinc peroxide	8 days later	12	Living
11	27	M	3	Extraction of lower molar tooth	Sulfa-thiazole	Yes	No	Bilateral	Local and Pentothal	Zinc peroxide	No	17	Living
12	52	M	2	Toothache in left lower jaw	Sulfanil-amide	No	No	Left side*	Pentothal	Azo-chloramid	No	23	Living
13	28	M	12	Extraction of lower molar tooth	Sulfanil-amide	No	No	Bilateral	Evipal	Boric solution	No	20	Living
14	10	M	4	Toothache of left lower jaw	Sulfa-thiazole	No	Yes	Left side	Local and Pentothal	Zinc peroxide	No	32	Living
15	29	M	5	Extraction of lower molar tooth	Sulfanil-amide	Yes	Yes	Right side	* Local and Pentothal	Chlorinate packs	No	23	Living
16	19	F	5	Toothache in lower jaw	Sulfanil-amide	Yes	Yes	Bilateral*	Local and Pentothal	Dakin's solution (half strength)	6 mo. later	12	Living
17	36	F	6	Extraction of 4 lower molar teeth	Sulfanil-amide	Yes	No	Right side	Local and Pentothal	Dakin's solution (half strength)	No	9	Living
18	26	F	2	Extraction of lower molar tooth	None	Yes	Yes	Bilateral*	Local and Pentothal	Dry gauze	2 mo. later	17	Living
19	17	M	4	Extraction of lower pre-molar tooth	Sulfa-thiazole	Yes	No	Left side	Local and Pentothal	Zinc peroxide	No	17	Living
20	58	M	2	None	Sulfathiazole and sulfadiazine	No	Yes	Bilateral	Local and Pentothal	Iodoform gauze	No	22	Living

*One submaxillary gland removed.

COMPLICATIONS

Respiratory obstruction has been cited as the most imminent and potentially dangerous complication of Ludwig's angina.¹ The employment of tracheotomy or preparation for tracheotomy as a preliminary to operation is the surest and most effective means of circumnavigating respiratory difficulties. One patient (Case 2) in the present series died on the operating table directly from respiratory obstruction.

The second and only other fatality (Case 6) was associated with tracheotomy. A preliminary tracheotomy was performed. The operation went well and convalescence was satisfactory until the third postoperative day, when profuse hemorrhage occurred in the tracheotomy wound. This was apparently due to a ligature's slipping from a small blood vessel that had been ligated at operation. Before the hemorrhage could be controlled, the patient had aspirated such a large amount of blood that he became cyanotic and dyspneic. He died two days later of bronchopneumonia, which appeared soon after the hemorrhage and seemed to result from the presence of retained blood and mucus in the air passages.

The decrease in complications parallels reduction of mortality in the previous series as compared with this one. Prompt and fearless employment of tracheotomy and immediate adequate drainage doubtless account for this reduction. The sulfonamide drugs have probably played a part in the good results, but their role is impossible to measure exactly.

TREATMENT

The aims of treatment, as previously stated,¹ are "to establish an adequate airway, to relieve tension, to secure drainage and to combat the infection by supplementary measures."

Surgery

We have come to believe that establishing an airway is of first importance. No doubt this can be accomplished in some of the early cases, through intubation, that is, catheterization of the trachea through the nasal or oral cavities via the larynx. If it can be done, this measure is sound and sufficient. However, it presupposes an early case with minimal swelling about the oral and pharyngeal cavities, and such cases are few, since the patients as a rule are not referred to the hospital until their plight is bordering on the desperate. Also, the services of an expert in the art of intubation are essential, and such experts are not plentiful outside of specialized centers. Intubation was attempted in 2 patients in this series. In both cases intubation was resorted to because of deep cyanosis and obstruction of the airway, which developed on the

operating table toward the end of the procedure. The tube was successfully passed in one patient (Case 11), who recovered. In the other (Case 2), intubation was not successful and the patient died. Anyone familiar with endotracheal intubation is aware of the fact that passage of the tube is often associated with severe spasm of the larynx. If intubation in Ludwig's angina is unsuccessful, the resulting spasm may easily cause an immediate fatality through asphyxiation. Tracheotomy would then be too late. Where it becomes necessary to establish an airway, tracheotomy exclusively is safer in view of these hazards associated with endotracheal intubation. The value of and indications for tracheotomy were discussed in some detail in the previous report.² Further experience with these cases has convinced us that the state of the airway cannot be accurately evaluated by the signs and symptoms ordinarily relied on. More important, it is impossible to predict the behavior of the airway under anesthesia, for spasm may intervene, completely obstructing what before operation seemed to be a fairly free passage.

These difficulties were partially recognized in the previous papers,^{1, 2} wherein exposure of the trachea preliminary to operation on the infected areas was advocated in cases where signs of respiratory difficulty were noted beforehand. This assumes that one can evaluate the present and future state of the airway on the basis of respiratory signs and symptoms, an assumption that we now know to be fallacious.

Accordingly, we have come to believe that in every case, prior to incising the suprathyroid region, a preliminary exposure of the trachea should be completed. For this purpose, a transverse incision 5 cm in length and 25 cm above the superior border of the sternum is made. A transverse incision is preferred because it avoids the infected tissues higher in the neck. Local anesthesia (with 1 per cent novocain) is employed. The anterior aspect of the trachea is cleanly exposed at about the level of the thyroid isthmus. This wound is then packed with vaseline gauze, protected with a sterile towel, and the main operation performed. If respiratory obstruction becomes apparent at any time, the pack is removed from the wound in the lower neck, the trachea is quickly incised, and a tracheotomy tube is inserted. Careful hemostasis, secured during the preliminary exposure of the trachea, assures one of a dry field through which the trachea can be entered. Oxygen may then be given by catheter through the tracheotomy tube and the main operation continued.

Whenever patients have respiratory obstruction previous to operation, as evidenced by dyspnea, cy-

nosis, orthopnea or crowing respirations, not only should the trachea be exposed, but tracheotomy should be completed before any other operative procedure is attempted. To do otherwise is to court death.

In 13 (65 per cent) of the cases in this series, preliminary exposure of the trachea was performed. In 9 of them, it was not found necessary to complete the tracheotomies. All these patients recovered. In 4 cases, tracheotomy had to be completed while the patient was still on the operating table. Three of these patients recovered and 1 (Case 2) died at the completion of the operation. Respiratory obstruction supervened at this point, apparently on account of spasm. Instead of immediately completing the tracheotomy, which could have been simply and quickly done since the trachea had already been exposed, endotracheal intubation was attempted, for some reason that is not clear. This precipitated further spasm and respiratory obstruction. The catheter could not be passed. The attempt at intubation was abandoned and the tracheotomy completed, but irreversible changes had already taken place, and the patient could not be revived. We regard this as a preventable death.

In 4 cases, tracheotomy was performed as a preliminary to the main operation, the preoperative clinical picture indicating impending respiratory obstruction. The operative course was uneventful in each of these cases. One of the patients (Case 6), already referred to, died from a hemorrhage in the tracheotomy wound. Such an accident is extremely rare in the experience of most surgeons. The possibility of its repetition is sufficiently remote so that we have no hesitancy in continuing to recommend tracheotomy when the clinical picture warrants it.

In the remaining 3 cases, the operation was performed without prior tracheotomy or preliminary exposure of the trachea. The operative courses were uneventful, and all patients survived. In view of wider and more recent experience, we should not be inclined to take such chances again in spite of the good results in these cases.

Surgical technic. Immediate surgical drainage is indicated in any case that has progressed to the point of fulfilling the diagnostic criteria of Ludwig's angina. The sulfonamide drugs, although doubtless of great benefit, have not altered our attitude in this matter. The arguments for immediate surgery were detailed in a previous report¹; the operative technic was likewise described fully. Therefore, only a brief outline of the surgical procedure will be included in this paper.

After preparing and draping the neck, an incision is made parallel to and 1.5 cm. below the body of the mandible, beginning 1 cm. in front of

the angle of the jaw and extending anteriorly to just beyond the midline, if the infection is unilateral. If the infection involves both sides of the neck, the incision is continued around almost to the angle of the jaw on the opposite side. It divides the skin, the superficial fascia and the platysma muscle. The deep cervical fascia and the mylohyoid and anterior bellies of the digastric muscles are also cut through. In this manner, the submaxillary and sublingual spaces are widely opened and drainage is thus secured. The submaxillary gland is in plain view and should be removed if it appears to be involved in the septic process. Sometimes pus is found above and posterior to the submaxillary gland. In such cases, the gland should be removed to facilitate drainage. At this juncture, the exploring finger lies directly under the mucous membrane of the floor of the mouth anteriorly and can be passed into the parapharyngeal space posteriorly. Pus will occasionally have dissected back into the latter space.

Postoperative dressings. In a few cases, at the completion of the operation, we placed from 5 to 8 gm. of sulfanilamide crystals in the depth of the wound and loosely packed the wound with iodoform gauze. Limited experience does not permit evaluation of this local use of sulfanilamide, but considering the types of organisms known to inhabit these wounds and the good results obtained with the drug in other wounds, further trial of this type of dressing is recommended.

The first dressing is changed at the end of twelve to twenty-four hours, all bleeding usually having ceased by that time. What type of dressing to use thereafter can best be answered by the bacteriologic studies. If only streptococci are reported from the wound culture, it is probably best to continue with the local use of sulfanilamide crystals, with an overlying saline-soaked gauze dressing. If Vincent's organisms are shown to be present, we strongly recommend shifting to zinc peroxide dressings. The latter must be carefully made and changed at least every four hours if good results are to be obtained. If properly managed, zinc peroxide dressings will yield a clean, odorless wound in an unbelievably short time. For the technic of these dressings, the reader is referred to the papers of Meleney.^{4, 5}

In order to obtain the necessary bacteriologic data on which to base future treatment, wound cultures as well as smears must be made at the time of operation. It is necessary to take the smears separately, for it is by this means that Vincent's organisms are demonstrated. They will not grow on ordinary culture mediums.

Secondary closure of the wound is advisable in some cases where the skin edges gape apart, but

this is not the rule. If dressings have been made skillfully, resuture should be feasible by the eighth day. Such closures were performed in 2 cases of this series on the eighth and twelfth postoperative days, respectively. In 3 other cases, the patients were readmitted several months later, when plastic procedures were carried out to eliminate the scars. If the wound edges are not approximating well, early resuture is simpler, saves the patient a second hospitalization, and gives a good cosmetic result. Incisions made for preliminary exposure of the trachea may be resutured on the third or fourth postoperative day, or as soon as it is clear that the potential need of tracheotomy has passed. It is, of course, assumed that it has not been found necessary to complete the tracheotomy in these cases.

A word regarding the care of the tracheotomy opening is not amiss. A suction machine at the bedside is essential so that the trachea and tube can be suctioned free of mucus or blood whenever such accumulations occur. The inner cannula of the tube should be removed and washed several times daily. The opening must be protected from contamination from the septic discharges of the wound above. Ordinarily, tracheotomy tubes can be removed on the third or fourth day, for the swelling about the pharyngeal and oral airways has usually subsided for the most part by that time. Obviously, it is desirable to remove the tube as soon as it can safely be done.

Use of Sulfonamides

We have been unable to control the disease in any case with sulfonamide therapy alone. In all cases in which sulfanilamide was used 2 gm. (30 gr.) was given on entry and 1 gm. (15 gr.) every four hours thereafter. In 1 case (Case 13) the patient was treated in the hospital for seven days with sulfanilamide. During this time, the disease progressed so as finally to require surgery. In 2 other cases (Cases 15 and 17), the patients were treated with sulfanilamide for three days, during which time each became worse. Both were operated on. Another patient (Case 20) grew worse at an alarming rate, so that radical operation was necessary in less than twenty-four hours. The findings on admission were minimal and a diagnosis of Ludwig's angina could not be made until the next day, by which time 3 gm. (75 gr.) of sulfanilamide had been administered. In view of these experiences, it is distinctly dangerous to convey the impression that chemotherapy alone will abort the disease and bring about a cure. This may happen in a few cases, but it is certainly not the rule. We regard the sulfonamide drugs only as valuable adjuncts to surgical treatment. They should not be

relied on alone in any fully developed case of Ludwig's angina.

Sulfonamides were administered either orally, parenterally or by both methods in 16 (80 per cent) of these cases. Sulfathiazole was used in 7 cases and sulfanilamide in 8. In 1 case, sulfathiazole was employed preoperatively and sulfadiazine postoperatively. In most cases, the dosage was 15 gr. every four hours. No superiority of any one drug over the others was noted, and it would be extremely difficult to establish such an evaluation, since the disease is relatively uncommon. Judging from what is known of the action of the various sulfonamides in relation to bacteriology, sulfathiazole or sulfadiazine appears to be preferable to the others for either oral or parenteral administration.

No complications due to chemotherapy were observed.

In 4 cases, no sulfonamide was administered. One of these patients (Case 2) was operated on shortly after admission and died on the operating table, so that there was no opportunity for such therapy. The other 3 patients recovered satisfactorily without the administration of sulfonamides. There is no tangible difference in the courses of the patients who received such therapy and of those who did not. However, we strongly recommend the use of one of the sulfonamide drugs on the basis of their more obvious beneficial results in inflammatory conditions elsewhere in the body, and because of the apparently universal presence of streptococci in the wounds of patients suffering with Ludwig's angina.

ANESTHESIA

In the previous communications,^{1,2} the choice of anesthetic methods was discussed at length. It was suggested that on the basis of experience then available, together with a knowledge of the obstructive changes that involve the airway, a combination of local anesthesia and Pentothal Sodium or Evipal is best. It is recommended that the trachea be exposed or tracheotomy completed under local anesthesia (local infiltration with 1 per cent procaine). This having been done, and an airway or potential airway thus assured, Pentothal Sodium should be administered intravenously and the incision and drainage carried out under the latter type of anesthesia, nasal oxygen being given during this second phase of the procedure. Procaine is injected only in the area of the tracheotomy, and none is used in the submandibular region. For complete details, the reader is again referred to the previous reports.

The intravenous barbiturates were employed in all 20 cases of this series—Pentothal Sodium in 19 cases and Evipal in 1. In 17 cases either tracheotomy or preliminary exposure of the trachea, per-

formed under local anesthesia, preceded the administration of Pentothal Sodium. One of these patients (Case 2) died on the operating table; this death has already been discussed. Since prompt completion of the tracheotomy would most probably have saved this patient, the death is attributable to faulty judgment rather than to the anesthetic agent. It has been stated above that in 3 cases where preliminary exposure of the trachea had been performed, completion of the tracheotomy became necessary during the operative procedure because of respiratory difficulties. That these difficulties arose from mechanical obstruction of the airway rather than from suppression of respirations by the anesthetic agent is evidenced by the fact that in each case tracheotomy was followed by immediate improvement. In 4 cases where tracheotomy was performed initially, no respiratory difficulties were noted at any time. This further substantiates our belief that Pentothal Sodium is not a dangerous agent in these cases if proper steps have been taken to provide a patent airway. In no case where the airway was patent was any respiratory difficulty experienced.

In 3 cases the operation was performed without preliminary exposure of the trachea or tracheotomy. No respiratory difficulties were encountered and all the patients survived. Pentothal Sodium was used in 2 cases and Evipal in 1 because the patient had received sulfanilamide for seven days prior to operation. It has been suggested that dangerous results may ensue from the administration of Pentothal Sodium to patients who have been receiving sulfonamides.⁶ However, in 3 other cases where sulfonamides had been administered up to 3 days preoperatively, Pentothal Sodium was used and no ill effect was noted. We do not believe that we have proved or disapproved the suggested incompatibility of Pentothal Sodium and the sulfonamides. However, we should have no hesitation in administering the former under such circumstances. It is perhaps safest to regard the question

as still unsettled. If Evipal is available, there is certainly no objection to its use.

SUMMARY

Experiences with Ludwig's angina in a series of 20 cases are related in view of the findings in 31 cases previously reported.

The mortality in the present series was 10 per cent, compared with 54 per cent in the earlier series.

Criteria for diagnosis are presented briefly.

Emphasis is placed on the role of the teeth and dental procedures as etiologic factors.

Streptococci were present in all cases, and both streptococci and Vincent's organisms in 8 of the 16 cases in which bacteriologic studies were made. Employment of both cultures and smears taken at operation is urged as a basis for the choice of dressings postoperatively. Zinc peroxide dressings are recommended when anaerobes are demonstrated.

Radical surgery as soon as the diagnosis is established is advocated.

The surgical technic is outlined. Preliminary exposure of the trachea or tracheotomy prior to operation is advised in every case. Intravenous Pentothal Sodium is recommended as the anesthetic agent of choice.

The use of sulfonamide drugs, either orally or parenterally, is strongly favored. Dependence on sulfonamides without surgery, however, is discouraged.

Under the regime advocated, the ordinary complications of Ludwig's angina have virtually been eliminated.

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CLINICAL NOTES

SURVIVAL FOR FOUR YEARS FOLLOWING DISSECTING ANEURYSM OF THE ABDOMINAL AORTA

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THE correct ante mortem diagnosis of dissecting aneurysm of the abdominal aorta is no longer an entirely adequate reason for reporting a case, except to emphasize the possibility of such a diagnosis, but the combination of a correct ante mortem diagnosis, recovery, and survival and economic usefulness for four years, death from a cause other than the aneurysm, and post mortem confirmation of the diagnosis makes the following case worthy of more than casual attention. Cases have been described where a "double barreled aorta" of obviously long duration has been found at autopsy, but in no such case, so far as I can find, has the condition been diagnosed during life and a survival period of four years determined.

CASE REPORT

J. A. H., a 57-year-old man, was admitted to the Lawrence General Hospital on February 1, 1938.

There had been persistent pain in the back since January 20, when, after watching some exciting boxing, the patient felt the sudden onset of severe pain between the scapulas, which spread to the substernal region. He was brought to the office where he paced the floor, obviously in severe pain. The temperature was 96°F, the pulse 80 and the blood pressure 260/140. The white-cell count was 8000. The lungs were clear and examination of the heart was essentially negative. Examination of the abdomen was negative except for slight tenseness in the epigastrium with no accompanying tenderness. The pain was severest in the back. There was no dyspnea, orthopnea, cyanosis, tachycardia, sweating, ashen pallor, nausea or vomiting. It was thought that the patient had a coronary thrombosis and he was given ¼ gr. of morphine sulfate intravenously, with complete relief of the chest pain but incomplete relief of the pain in the back. He was taken to the home of his sister in law, where he was again given, within ½ hour of the first dose, ¼ gr. of morphine sulfate intravenously, but still without complete relief. He was confined to bed, given morphine whenever necessary for his pain, a liquid and soft solid diet and special nursing care.

On the next day the temperature began to rise and the white-cell count was 12,000. On January 22 the temperature was still elevated, the white cell count was 18,000 and an electrocardiogram showed a diphasic T wave in Lead 4 but no definite sign of coronary disease (Dr. Joseph Nicholson). The blood pressure, which had been taken every 2 hours gradually fell to 152/98 on the afternoon

of January 21, and then gradually rose to 200/120. On January 22 the diagnosis of dissecting aneurysm of the aorta was made.

The patient continued to have severe pain requiring medication every 3 to 5 hours; the pain gradually descending until it localized in the lower back. He perspired freely and complained that back rubs were unpleasant and painful, although deep pressure was not disturbing. Lying on his back increased the pain.

The urinary volume gradually decreased and on January 23 the patient passed only 390 cc. of highly concentrated urine containing a very slight trace of albumin, no sugar and a large number of granular casts with an occasional red and white cell. Repeated urine specimens taken later contained a similar amount of albumin although somewhat fewer casts. After January 23, the urine volume increased.

On January 27, a thrill was felt high in the epigastrium, slightly to the left over a palpable pulsation of the abdominal aorta. Over the aorta, especially in its upper part, was a loud bruit, systolic in time. After examination of the epigastrium the pain was much worse.

The rectal temperature persisted at about 101°F, with a slight tendency to drop within the last few days before admission. Between the onset of illness and admission to the hospital (12 days) the patient received 12½ gr. of Pantopon and nearly 4 gr. of morphine sulfate, not counting the two initial ¼ gr. doses.

The patient's father died at 55 years of unknown causes. The mother died of dropsy. One brother died at 50 years of shock. Two sisters were living and well. The patient's wife died of high blood pressure at 50 years. Two children were living and well. One child was born dead, and there had been two miscarriages. The patient had had a nervous breakdown lasting 6 weeks, 10 years previously.

The patient was able to lie on his back without acute distress or pain. He appeared somewhat drawn and showed signs of having lost some weight recently. The lungs were normal. The heart was somewhat enlarged to the left, and the supracardiac dullness was 8 cm. wide in the 2nd interspace with its right border at the right border of the sternum. The sounds were of good quality. The aortic second sound was increased and was greater than the pulmonic. The rhythm was regular. There was a soft systolic blow at the apex, but no murmurs at the base. Examination of the abdomen was negative except for pulsation of the abdominal aorta throughout its length. A loud systolic bruit could be heard over the aorta with diminishing intensity in the lower abdomen. In the epigastrium, just to the left of the midline, there was an easily palpable thrill, synchronous in time with the bruit. The extremities were normal.

Repeated x-ray films were negative. The red-cell count was 4,370,000 with a hemoglobin of 89 per cent (Sahli). On entry, the white-cell count was 20,200, with 83 per cent neutrophils, 1 per cent eosinophils, 8 per cent small monocytes and 8 per cent large monocytes. On February 21, it was 9200. The nonprotein nitrogen was 33.6 mg. per 100 cc. A blood Hinton test gave a negative reaction. The urine on admission was amber and acid, with a specific gravity of 1.022, a slight trace of albumin and no sugar. On February 13 it was yellow and acid, with a specific gravity of 1.024.

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slightest possible trace of albumin and no sugar. There were a moderate number of white blood cells and an occasional epithelial cell in the sediment.

On February 16, or 27 days after onset, the patient became sufficiently free of pain so that morphine was no longer necessary; the thrill over the aorta was no longer palpable. On March 1 he was allowed to sit in a chair and later to take a few steps to the bathroom. He was discharged by ambulance to a convalescent home on March 4. The bruit over the aorta was still audible.

About 6 months after onset, the patient gradually resumed his duties as foreman in a textile mill and continued reasonably well until February 10, 1941, when he had a pontine cerebral hemorrhage, with severe headache, mental confusion, nausea, vomiting, contracted pupils, slowed respirations, left facial palsy, left deviation of the tongue, partial deafness and at one time a blood pressure of 300/130. He returned to work in 2 months and continued until January 20, 1942, when he had his first attack of severe paroxysmal dyspnea. He died on January 23 in a similar attack.

Autopsy (Dr. Donald A. Nickerson). The heart was moderately enlarged, measuring 12.5 by 10.8 by 7.5 cm. The epicardial surface was smooth and glistening, and covered by a small amount of fat. The myocardium was firm and reddish-brown, showed relatively little gross scarring and was not remarkable except that the left ventricular wall presented a definite degree of concentric hypertrophy, so that the wall averaged 2.0 cm. in thickness. The chambers were lined by smooth and glistening endocardium, and the valves were normal except for a few small plaques at the bases of the aortic leaflets. The coronary ostia were present, and the vessels showed moderate atheromatous deposits, with narrowing of the lumens but no evidence of complete occlusion.

The aorta was dissected out with the heart to the bifurcation of the iliac vessels. It was of approximately average size as it lay in situ. When opened the thoracic portion was of average width and showed scattered atheromatous plaques, which were more numerous in the distal portion; these, for the most part, had a yellowish-gray, raised appearance, with occasional foci of calcification. In the lumbar portion, at a point 3.5 cm. above the celiac axis artery, there was an oval aperture 2.0 cm. in length and 0.6 cm. in its greatest width, the axis of which was parallel to that of the aorta. Its margins were lined by somewhat rolled, curled, glistening, yellowish-tan tissue, and it led into a sac that paralleled the entire remaining portion of the aorta. Proximal to the opening of the dissecting aneurysm there was a firm, semicalcified, bulging mass measuring 3.5 by 3.0 cm., partially filled with laminated blood clot in its upper margin but for the most part covered with smooth, glistening and granular yellowish-gray tissue. From this point downward there was a partially encircling, dissecting sac, the lining surface of which was ragged, granular, yellowish-gray and marked by numerous atheromatous plaques. The aorta in this region showed somewhat more marked atheromatous change than it did in the thoracic portion, with occasional longitudinal furrowing, but there was no occlusion of the orifices of the major vessels or pearly-gray plaques about their mouths. The degree of atheromatous change was somewhat more marked in the aorta than in the dissecting aneurysm. At the bifurcation of the vessels the sac of the dissecting aneurysm passed under the aorta and coursed beneath the origin and proximal 4.5 cm. of the right iliac artery. At that point there was a re-establishment of a

common channel as the channel of the dissecting aneurysm dissected upward and joined with the iliac artery.

SUMMARY

A case of dissecting aneurysm of the abdominal aorta is described in which the patient recovered and was able to work for nearly four years. The original diagnosis was confirmed at autopsy.

5 Third Street

A SIMPLE TIDAL-DRAINAGE UNIT

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BOSTON

AS a result of the war, the subject of tidal drainage is beginning to receive more widespread attention than formerly. This has been occasioned by the increased interest that has centered about the management of patients with traumatic lesions of the spinal cord.

The use of tidal drainage to manage the neurogenic bladder resulting from this condition was introduced by Munro and Hahn¹ in 1935. This and the other indications for the use of tidal drainage will not be discussed in this paper. Munro,² in 1936, designed an apparatus for tidal drainage, which has since been modified by others (Hyams and Buchtel,³ Vary⁴ and Bellis⁵). Each modification has been designed to simplify the complexity of the apparatus and the care that it requires.

It is the purpose of this paper to present an apparatus that operates on the same principle. It is easy to construct and constitutes a single piece of apparatus that can be readily operated by one unfamiliar with the working principles of tidal drainage.

The apparatus described below is suitable for hospital use and allows easy cleansing and sterilization. However, the use of nonbreakable materials would make it applicable for field-hospital work as well.

An apparatus designed for tidal drainage, besides being simple in construction, should embody the following characteristics: it should be possible for the bladder to be filled to any desired tension, and to be completely emptied after this pressure has been obtained; and it should be possible to allow a period of rest before the bladder is again filled.

METHOD OF CONSTRUCTION

An apparatus that fulfils all these requirements can be constructed with glass tubing of two different diameters. It can be built to any size, de-

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pending on the volume and pressure desired. For irrigating the urinary bladder, the following specifications have been found to be satisfactory.

A piece of 25 mm glass tubing 62.5 cm in length is closed at each end with a No. 4 two-holed rubber stopper. This is referred to as the column. A

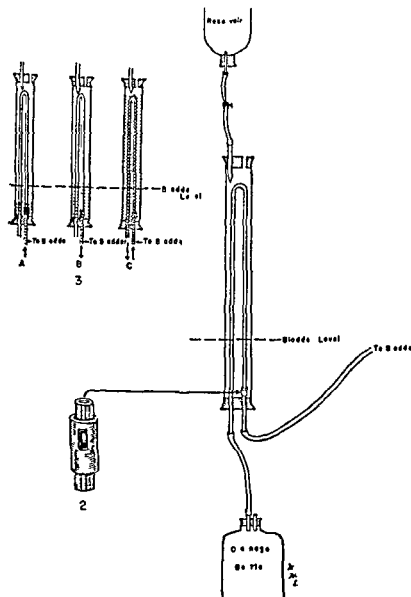


FIGURE 1

- 1—Complete unit 2—Detail of siphon adjustment
3—Different phases of operation (a) resting
(b) filling (c) emptying

piece of 6 mm glass tubing, 110 cm long, is bent 50 cm from one end, so that it forms a U with arms of unequal length, and so that it will fit with in the column. This is the siphon. Its longer arm projects through one hole of the lower stopper (Fig. 1-1), and is adjusted in this position so that the shorter arm ends 12 cm above the stopper directly over the second hole. A 75 cm piece of 6 mm glass tubing is then placed in the second hole, so that the upper end is separated from the short end of the siphon by 3 mm. A segment of 6-mm rubber tubing 19 cm long is used to connect these ends. A narrow window 6 mm long is cut in one side of the rubber tube. The bore of the tube is then stretched so that when in position it can be easily moved up and down. By varying the size of the portion of the window that overlies the gap between the two tubes, one can adjust the

size of the aperture between the siphon and the column (Fig. 1-2). An adjustment producing a hole 1 or 2 mm in diameter is satisfactory.

At the upper end of the column, one of the two holes in the stopper is left open to act as an air vent. The other hole contains the glass inflow tube, which allows fluid to enter the column. The end of this tube is drawn out to a diameter of 1 or 2 mm, so that the rate of inflow can be observed and regulated.

METHOD OF OPERATION

A large reservoir containing the irrigating fluid is connected to the inflow tube with rubber tub-

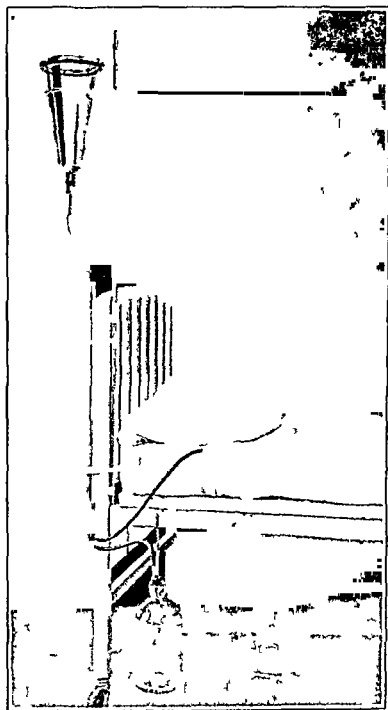


FIGURE 2 Apparatus Connected for Use

ing, and controlled with a constricting clamp (Fig. 2). The short glass tubing at the base of the column is connected to the bladder, and the long arm of the siphon, which protrudes through the stopper, is connected to the drainage bottle, where it ends as a short piece of glass tubing in another two-holed stopper.

When the clamp is opened fluid flows into the column. The fluid has direct access to the bladder through the hole in the side of the siphon. When the fluid level in the column rises above bladder level, as in Figure 1-3b, the bladder begins to fill and the pressure within the bladder rises. This pressure may be observed and measured in the short arm of the siphon.

When the fluid in the column and that in the short arm reaches the level of the siphon curve, the fluid flows into the descending siphon arm and the bladder is emptied. Simultaneously the fluid is siphoned from the column through the small hole in the side (Fig. 1-3c). The emptying time of the column must be sufficiently long to allow the bladder to empty completely. When the column is empty, air enters the siphon and breaks the circuit. Then the level of the fluid in the column is below that of the bladder (Fig. 1-3a), and if the emptying has been incomplete, the column immediately fills to bladder level. In this event, the hole in the side of the siphon must be decreased in size so that the column empties

more slowly. The bladder remains at rest until the fluid in the column again reaches bladder level.

The hole in the side of the siphon should be as large as is compatible with complete emptying of the bladder, for excessive constriction makes the apparatus more easily tripped by sudden changes of abdominal pressure.

Intravesicular pressure is adjusted by changing the level of the entire unit.

SUMMARY

The construction of a simple, inexpensive apparatus for tidal drainage is described, and its use is discussed.

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MEDICAL PROGRESS

ISOTOPES IN MEDICAL INVESTIGATION AND THERAPY*

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THE preliminary period in which radioactive isotopes were a novelty and each newly discovered radioactive element was immediately fed to a few rats, its distribution in various bodily tissues and rates of excretion in urine and feces determined, and the findings promptly published is drawing to a close. Today the isotope-tracer technic is no longer a novel toy to be employed in new and unique situations, but a precise and irreplaceable method of studying complex problems of metabolism, physiology and disease. Investigators who have spent many years applying the classic investigative procedures are now adapting the isotope-tracer method to their research, and as a consequence are making advances that would have required years to achieve or have been impossible with the methods previously at their disposal. The stable or heavy isotopes (which can be detected because of the differences in their atomic weights)

have been used primarily as markers in organic molecules, and have made their greatest contributions in the study of the intermediary metabolism of fat, protein and nitrogenous substances. Unstable or radioactive isotopes of almost all the elements have been made by cyclotron bombardment or atom-smashing. To date their greatest usefulness has been in investigations of the metabolism of ions and inorganic substances.

It should be emphasized that atoms, not molecules or compounds, are made radioactive. Only by incorporating such atoms in molecules, compounds or tissues can the latter be labeled with a radioactive substance. Incorporation of isotopes in molecules or compounds can be accomplished by chemical methods (for example, the labeling of sodium chloride by making it from radioactive sodium) or by allowing an organism to use an isotope as a building stone for the formation of a complex organic substance or a tissue that will contain the labeled atom. Thus, if an anemic subject is fed radioactive iron, this isotope is built into hemoglobin contained in newly formed eryth-

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rocytes, and serves to label not only the hemoglobin molecule but the erythrocyte itself.

The medical applications of these labeled substances, varying in complexity from simple inorganic ions to entire physiologic units such as the erythrocyte, are extremely numerous and the literature reporting them now runs into some four hundred articles. The impracticability of summarizing such a number of data is obvious, and consequently only those subjects that have appeared to be of immediate clinical interest are reviewed in this report.

STOMACH

Gastric secretion and absorption are poorly understood, in spite of the intensive investigations of gastric physiology made during the last fifty years. The isotope-tracer technic appears to be an ideal means of following the transfer of ions and molecules across the gastric mucosa, since the few experiments already performed by this technic have yielded striking and valuable information.

Cope and his associates have continued their studies of gastric physiology using radioactive sodium and heavy water as tracer substances. In their first series of experiments, they¹ introduced solutions containing radioactive sodium in the form of sodium chloride into the gastric pouches of dogs, and followed the appearance of the radioactive material in the blood stream. Significant amounts of sodium were absorbed within fifteen minutes, but the total amount absorbed varied remarkably depending on which portion of the stomach had been used in making the pouches. In a period of one hour only 1 to 7 per cent of the radioactive material was absorbed from the pouches made in the body or acid-secreting portion of the stomach, whereas as much as 50 per cent was absorbed from the alkaline-secreting antral pouches. Much less sodium was absorbed from the body of the stomach during the secreting phase than during the resting phase, but the state of secretory activity had little effect on absorption from the antral region. Variations in the osmotic pressure of the sodium chloride solutions or in the electrolyte concentrations in the blood serum had no significant effect on the absorption.

The absorption of water from the stomach was studied by determining the rate of disappearance of heavy water (water containing the heavy isotope of hydrogen) from the gastric pouches.² Absorption from both body and antral pouches was rapid, 50 per cent of the heavy water being taken up in approximately twenty minutes, although none of the labeled material remained in either pouch after two hours. The functional state of the gastric mucosa had no effect on the absorption.

These interesting and extremely important experiments indicate the futility of assuming that analyses of the gastric contents give an adequate picture of the secretory activity of the stomach. The concentrations of various constituents in the gastric contents actually represent the result of an equilibrium between the simultaneous processes of secretion and absorption. The rapid transfer of water through the gastric mucosa easily explains the constant state of isotonicity of the gastric contents, and makes it unnecessary to assume that the secretory products of the mucosal cells are isotonic at the time of delivery into the stomach.

Other evidence that the stomach can take an active part in absorption is given in the experiment reported by Hahn and Whipple³ in which a solution containing radioactive iron was placed in the gastric pouch of an anemic dog. A high percentage of the iron was absorbed and appeared in the circulation. As a matter of fact, the absorption of iron from the isolated pouch was as great as would have been expected from the entire enteric canal of the animal.

Studies of the secretion of the radioactive substances by the stomach have not been so extensive or so carefully controlled as studies of absorption. Brunschwig, Schmitz and Slottin⁴ detected radioactive chlorides in the gastric secretion of stomach pouches within a few seconds after the labeled material was injected intravenously. They attempted to demonstrate the presence of a specific inhibitor of gastric acid secretion in the alcoholic extracts of gastric juice from a patient with pernicious anemia. Although the intravenous injection of this extract prevented secretion of chloride ions by the stomach for a period of forty minutes, there was extreme inhibition of all gastric secretion. Since it is well known that many adverse conditions—for example, the intravenous injection of foreign proteins—almost completely arrest gastric secretion, it does not seem reasonable to conclude on the basis of these experiments that the extract from achlorhydric gastric juice has a specific inhibiting effect on the secretion of chloride ions.

Radioactive chloride appeared rapidly in the gastric secretion of 5 patients with achlorhydria, but no definite evidence as to the acidity of the secretion was presented. Brunschwig, Schmitz and Slottin concluded that chloride ions could pass readily into the gastric juice independent of free acid, and that free-acid formation by the gastric mucosa is not dependent on the availability of chloride ions. Although the data presented do not justify these conclusions, the findings are sufficiently suggestive to merit repetition and extension of this type of experiment.

THYROID GLAND

Radioactive iodine has afforded a means of determining the exact role of iodine in the complex metabolism of the thyroid gland, and in addition has served as a tool for studying the effects of various hormones on this gland. It also offers considerable promise as an effective nonsurgical form of therapy for hyperthyroidism.

The remarkable ability of the thyroid gland to accumulate iodine has been clearly shown by several investigators.⁵⁻⁷ In contrast to other tissues in the body, the thyroid gland rapidly removes iodine from the blood stream, building up the total concentration of the material in the gland tissue to levels five to ten thousand times greater than those existing in the blood. Other body tissues take up iodine in amounts accounted for by simple diffusion, rapidly losing the element as soon as the blood level falls. There is a definite saturation level for iodine in thyroid tissue, however, and when this concentration is exceeded, further iodine can enter the gland only by diffusion. This excess iodine is rapidly lost as soon as the concentration of iodine in the blood stream decreases. Leblond and Süe⁸ found that 10 mg. of iodine per 100 gm. of fresh tissue was adequate to saturate the thyroid glands of rats, whereas the similar value for guinea pigs was 20 mg. They also believed that these animals utilized this amount of iodine every three days. If similar amounts of iodine should be required by the human gland, the daily requirement would be much greater than is indicated by present estimates.

The thyroid gland shows marked affinity for the other halogens as well as for iodine, since thyroid tissue selectively retains bromine⁹ and the newly discovered halogen, eka-iodine or element 85.¹⁰ As a matter of fact, one of the procedures employed for the identification of this newly discovered element was the demonstration of its localization in the thyroid gland in a manner similar to that of the known halogen, iodine. The importance of this localization from the standpoint of medicine is evident when it is pointed out that the new element localizes readily in hyperplastic thyroid tissue and that the radiations that it gives off are extremely powerful alpha particles. These particles produce a tissue ionization (an index of the degree of tissue destructiveness) more than two hundred times greater than the ionization produced by the beta radiation of radioactive iodine. It appears not unlikely that this element will prove valuable in the treatment of Graves's disease.¹⁰

Once radioactive iodine has reached the thyroid gland, it is rapidly converted into diiodotyrosine and thyroxine, as much as 70 per cent of the total

thyroid radioactive iodine having been found as diiodotyrosine and 22 per cent as thyroxine four hours after the material was fed to rats.¹¹ The ability of thyroid tissue to perform this conversion is dependent on the integrity of the glandular structure as well as on enzyme systems, for although slices of thyroid tissue rapidly converted radioactive iodine to diiodotyrosine and thyroxine in vitro, mincing of the tissue greatly reduced the rate and extent of this conversion, while homogenization completely destroyed the ability of the tissue to form thyroglobulins.¹² Mann, Leblond and Warren¹³ have shown that although inorganic iodine exists as such in the normal non-iodized thyroid gland, it is not the major precursor of either diiodotyrosine or thyroxine. This finding indicates that the conversion of injected radioactive iodine to diiodotyrosine takes place at the level of the thyroid cell membrane and suggests that diiodotyrosine is the natural precursor of thyroxine. From data on the relative rates of uptake of radioactive iodine as diiodotyrosine and thyroxine, these investigators estimated that in the dog 1.55 per cent of the thyroxine content of the thyroid gland is formed each hour.

Hertz and Roberts¹⁴ used radioactive iodine as an indicator to study the effect of thyrotropic hormone on thyroid physiology. They induced hyperthyroidism in rabbits by administering anterior-pituitary thyrotropic hormone. Radioactive iodine was then injected intravenously and the gland was subsequently assayed for its content of radioactivity. The uptake of radioactive iodine was correlated with the size of the gland, the height of the acinar cells and the basal metabolic rate of the animals. Although all these factors varied in the same direction, the ability of the cells to assimilate iodine did not always parallel the other functions. The basal metabolic rate, the cell height and the size of the gland showed initial rises in response to hormonal stimulation, reached a maximum, and subsequently declined. The ability to concentrate iodine showed a slight lag. The rate of decline was accelerated by the therapeutic administration of iodine, and the cell height, basal metabolic rate and ability to assimilate radioactive iodine fell below normal. When iodine was not administered therapeutically, a functional exhaustion of the gland developed: the cells showed involutional changes, the basal metabolic rate dropped below normal, and the size of the gland decreased markedly. In spite of these changes, the rate of iodine collection was still greater than normal.

These excellently planned and executed experiments clearly demonstrate that the results of the administration of thyrotropic hormone may be re-

garded as an initial stimulation followed by involution if iodine is administered, or by an eventual functional depression after prolonged hormonal stimulation. These data lend strong support to the concept that the thyroid gland shows a varying ability to collect iodine in various states of stimulation, with higher thresholds corresponding to the greater degrees of stimulation, and decreasing thresholds indicating conditions of involution or functional depression.

Other observations⁸ on the effect of thyrotropic hormone showed that the increased uptake of iodine by the hyperplastic thyroid tissue was due in some extent to a relative increase in the number of cells per unit of thyroid mass (which occurred because of a decrease in the amount of colloid in the acini). The increased iodine uptake was explained to an even greater degree, however, by an actual increase in the efficiency or activity of the cells. Overstimulation of the gland with massive doses of hormone decreased its capacity for iodine utilization, presumably because the excessive rate of growth (indicated by numerous mitoses) inhibited the functional capacity of the cells.

Radioactive iodine has been used clinically to determine the rate of assimilation of iodine by the thyroid gland. In general, the human gland was found to behave in a fashion similar to that already described in experimental animals. The rate of uptake and the total amount of iodine assimilated depended primarily on the gland's state of functional activity as indicated by the basal metabolic rate.¹⁵⁻¹⁷ These findings suggest the possible therapeutic application of radioactive iodine to hyperthyroidism, a subject that will be considered subsequently.

PLACENTA

Except for the fairly obvious fact that the fetus receives its nutrition from the maternal circulation through the placenta, remarkably little is known about the transfer of substances across it. Does the placenta act as an inert membrane or filter between the maternal and fetal circulations; or does it modify the transmission of substances by contributing energy to the process, thus acting as a secretory organ? Does the permeability of the placenta vary with the period of gestation? Is variation in placental transfer related to morphologic change in the placenta, to variations in its size or to variations in the growth rate of the fetus?

In an attempt to answer these and other questions, Flexner and Gellhorn^{18, 19} studied the transfer of radioactive sodium and heavy water across the placentas of several species of animal during the last half of gestation. These substances were

used as indicators of placental transfer because they are essential to animal growth and metabolism and because their behavior in the body is not complex. In these investigations, heavy water or radioactive sodium in the form of sodium chloride was injected intravenously into the mother. The fetuses were removed by abdominal hysterotomy an hour after the injection, at which time the fetal and placental weights were observed. Finally, the concentrations of the heavy water and of the radioactive sodium in the maternal blood plasma and in the ashed remains of the fetus were determined. Equilibrium of distribution of water between the maternal circulation and the fetus was established after thirty minutes, although equilibrium between maternal intravascular and extravascular fluids was reached in seven minutes. Similar values for distribution of sodium were four or five hours between mother and fetus and only five to thirty minutes between maternal intravascular and extravascular fluids. These findings indicate that the placental transfer is a much more complex process, and a considerably slower one, than simple exchange across a vascular epithelium. The marked difference in rate of transfer between water and sodium has been accounted for by assuming a differential permeability of the placenta for water and for sodium.

By correlating the rate of transfer of sodium per gram of placenta with the stage of gestation, it was found that the ability of the placenta to transfer sodium increased greatly during the course of gestation, by as much as sixty-seven times in the goat's placenta during the last half of gestation. This increase was associated with a decrease in the number of cellular layers of the chorionic villi and with a thinning of the remaining cells. A drop in transfer rate occurred just before term, and was associated with thrombosis of the maternal vessels and infarction of the placenta.

The placental transfer rate varied markedly with the animal species, so that it was possible to correlate this variation with the morphologic type of placenta characteristic of the species. The greater the number of tissue layers in the placenta, the lower was the unit transfer rate. For example, the unit transfer rate of the rat's placenta with three tissue layers was three hundred and twenty times greater than that of the sow's with six tissue layers.

The rate of transfer of sodium to the fetus was directly dependent on the relative growth rate of the latter. When the unit weight of the fetus was reproducing itself rapidly during the early stages of gestation, the transfer rate was high. During the later stages of gestation, when the relative growth

of the fetus was not so great, the transfer rate was correspondingly low.

These findings allow the postulation of a fundamental principle that appears to underlie all placenta transfer, namely, the rate of supply of a substance to a unit weight of fetus parallels the rate at which that unit weight of fetus is reproducing itself. It seems quite probable that any marked variation from this rate of placental transfer would have disastrous results on the fetus, and conceivably on the mother as well.

The transfer of water and sodium to and from the amniotic fluid was studied by the same technics as those employed in the placental investigation.²⁰ Contrary to the generally accepted belief that the amniotic fluid is relatively stagnant, the findings indicated that a volume of water equivalent to the total volume of amniotic fluid flows into and out of the amnion about once an hour in the early stages of gestation, and about once each forty minutes during the later stages. Although no information was obtained concerning the principal site of formation of the amniotic fluid, the rapidity of this exchange makes it appear highly improbable that fetal urine contributes materially to its formation. The difference in rates of transfer of sodium and water across the placenta was also observed in their transfer into the amniotic fluid, water being replaced about fifty times more rapidly than sodium.

Considerable speculation has arisen regarding the method by which iron is transferred to the fetus from the maternal body. The most commonly accepted hypothesis is that maternal erythrocytes are broken down in the placenta and that iron is freed from hemoglobin combination, transported across the placenta by macrophages, and subsequently released into the fetal system. The investigations of Pommerenke and his associates²¹ cast serious doubt on the necessity for assuming such a complex mechanism, since they were able to show transportation of demonstrable quantities of radioactive iron to the fetal plasma within forty minutes after the mother had ingested a single dose of radioactive iron. The rapidity of such transfer indicates that the blood plasma is probably the means of transport of iron to the fetus, and that iron may pass from maternal to fetal plasma across placental membranes by a process of diffusion. In human fetuses obtained from therapeutic abortions performed on mothers who had ingested radioactive iron prior to delivery, the greatest portion of radioactive iron was transferred to the fetus dur-

ing the latter months of pregnancy. This iron was rapidly incorporated in fetal erythrocytes, although appreciable amounts could be demonstrated in the fetal liver.

Phosphorus is apparently transferred across the placenta mainly as the inorganic phosphate, since large quantities of phosphate rapidly appear in the fetus when inorganic sodium phosphate is injected, but only minimal quantities can be detected in fetal tissues after injection of the mother with radioactively labeled phospholipid.²²

(To be concluded)

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**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL**ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor***CASE 29141****PRESENTATION OF CASE**

A sixty-nine-year-old housewife entered the hospital because of epigastric pain and persistent vomiting.

Approximately twenty years before admission she suffered with typhoid fever, from which she apparently made a complete recovery. However, ever since then she had been bothered by attacks of biliousness, often following fatty foods, that usually occurred two to four times a year and lasted approximately one day. These attacks were characterized by dull pain in the midepigastrium and right upper quadrant, which occasionally radiated to the precordium and along the medial aspect of the left upper arm. During some attacks she vomited almost continuously for twenty-four hours. The vomitus consisted of recently ingested food and bile-stained fluid. She had never had chills, fever, dyspnea, palpitation, jaundice, tarry or acholic stools or dark urine. Ten years before entry x-ray studies at a community hospital failed to demonstrate any abnormality of the gall bladder or stomach.

Four days before admission, following a meal that included bacon, she developed a severe, steady midepigastriaic pain that radiated to the precordium and left arm. Several hours later she vomited greenish material. Vomiting and pain persisted and on the day of entry the vomitus was ejected with considerable force. Since the onset of this illness she had not moved her bowels. An enema failed to relieve her. There was no dysuria, hematuria or nocturia.

The family history was noncontributory. A fibroid uterus was removed twenty-five years before entry. The patient had suffered with rheumatoid arthritis of both knees for two years.

Physical examination disclosed a well-preserved woman who was obviously quite uncomfortable. The skin was loose and quite dry. Examination of the lungs was negative. The apex of the heart was percussed 9 cm. to the left of the midsternal line in the sixth intercostal space. At times the apical rhythm seemed slightly irregular and suggested a gallop rhythm. The abdomen was soft; no masses were felt, and no tenderness was elic-

ited. Peristaltic sounds were absent. Pelvic and rectal examinations were negative.

The blood pressure was 110 systolic, 76 diastolic. The temperature was 97°F., but eight hours later rose to 100.2°. The pulse was 90, and the respirations 20.

Examination of the blood revealed a red-cell count of 5,630,000 and a white-cell count of 30,400 with 90 per cent polymorphonuclear leukocytes. When repeated ten hours later the white-cell count was 24,600. The urine sediment contained 1 or 2 white cells and occasional granular and hyaline casts per high-power field. A flat x-ray film of the abdomen showed a loop of dilated small intestine in the left midabdomen. One soft-tissue mass that lay in close contact with the lower pole of the right kidney measured 10 cm. in length and 6.5 cm. in width. There was another, poorly defined, soft-tissue mass arising from the pelvis that was somewhat irregular in outline.

Approximately fifteen hours after admission an exploratory laparotomy was performed under local anesthesia. The abdomen was opened through a left paramedian rectus-splitting incision. Loops of dilated jejunum were immediately encountered and these were followed to a 7.5-cm. knuckle of bowel that was caught under a firm fibrous band in the left lower quadrant. After the band was divided, the bowel regained color and peristaltic waves crossed the damaged segment of bowel. No resection was performed. The patient seemed quite satisfactory after return to the ward, but twenty-four hours later she became incontinent of urine and feces and began to vomit almost constantly, in spite of gastric suction. Attempts to pass a Miller-Abbott tube were unsuccessful. Eight hours later both legs seemed cold. No femoral, popliteal, dorsalis pedis or posterior tibial arterial pulsations were felt in either leg, and the legs were mottled as high as the upper thigh. Examination of the heart and lungs was unchanged. Peristaltic sounds were audible. Heparinization was begun, and one ampule of Spasmalgin was given every six hours.

The next day the patient was drowsy but could be aroused. The status of the legs remained the same. The urinary output was fairly good. Peristaltic sounds were absent. She was given a 500-cc. blood transfusion. The following day, the third postoperative day, she became comatose, passed bloody stools and died. The legs remained cold and bloodless, and the upper thighs were livid.

DIFFERENTIAL DIAGNOSIS

DR. E. PARKER HAYDEN: This is an interesting history with many possibilities. Let us go back

to the beginning. The patient was known to have had typhoid fever, and later had some attacks which, according to the description, sound like gall-bladder attacks. On the other hand the pain did radiate to the middle aspect of the left arm, at times, which suggests heart attacks. X-ray studies of the gall bladder and stomach in an outlying hospital were negative, but we do not know whether a Graham test was included or how reliable the x-ray reports were. She vomited continuously during these attacks, for twenty-four hours at a time.

The recent attack started four days before entry and followed a meal of high fat content. This may have been another gall-bladder attack similar to those the patient had had in the past, since there was the same type of radiation. On the other hand we do know, from the report of the operation, that definite obstruction was found in the small bowel, which was evidently considered to have been due to an internal hernia. With that knowledge it seems reasonable to suppose that the recent attack was due to intestinal obstruction even though the description of this attack is similar to those that occurred over a period of years.

On entrance to the hospital the patient was dehydrated. The heart was apparently not normal—just how abnormal, it is difficult to be sure from the description. The fact that peristalsis was absent makes one hesitate to interpret this as an attack of mechanical small-bowel obstruction, despite a description of what appears to have been a herniation, with visualization of the loop in an effort to see whether it was likely to survive or should be resected. These two findings do not go well together.

The uterus had been taken out sometime before. We have x-ray evidence of two soft-tissue masses, one below the right kidney and one arising from the pelvis. It does not say whether the latter lay more on one side than on the other. The woman may have had two ovarian cysts that developed after hysterectomy and had nothing to do with the present story. On the other hand, the shadows may represent a tumor that did have something to do with the present story. I am rather inclined to discount this finding, however. Apparently there was some degree of polycythemia, which brings up the possibility that she had an associated stomach ulcer—there being a fairly high incidence of gastric ulcers in polycythemia. The white-cell count was 30,000, out of proportion to the temperature, which, according to the history, never went above 100.2°F. The white-cell count dropped the following day to 24,600.

There seems to be little doubt that there was obstruction in the abdomen and that it was defi-

nately relieved by operation. Things were going nicely so far as the operation was concerned. Whatever killed this woman seems to have developed postoperatively. One naturally thinks of the possibility of her having developed a mesenteric thrombosis, inasmuch as there was diminished circulation in that loop of bowel at operation, and because of the red-cell count which seems adequate to have supported a diagnosis of mild polycythemia in a woman. Against the possibility of mesenteric thrombosis is the fact that on the day before she died she had audible peristalsis, although she could have had a thrombosis that had not progressed to the point of eliminating peristalsis. The abdomen was silent on the last day. Judging from the fact that she had received heparin she was considered to have thrombosis somewhere, but we know that she had in her legs either a rapidly progressive thrombosis or a large embolus at the bifurcation of the iliac arteries.

I find it extremely difficult to make a diagnosis on this history, but it seems to me as though the woman probably did not have a mesenteric thrombosis, but that her death was associated with an extensive disturbance in circulation to both extremities, with nothing acute within the abdomen. What the thrombosis was due to is difficult to say; she probably had some degree of polycythemia and developed thrombosis or embolism on the lower extremities. If it was an embolus it may have come from the heart or from some more obscure area. I really am quite at sea on the case, and doubt if I can make an intelligent diagnosis.

DR. GEORGE W. HOLMES: The shadows that I am pointing out represent the dilated small bowel. The loops are not only dilated but also show increased peristaltic activity. That suggests obstruction and is not the appearance seen in paralytic ileus.

DR. LELAND S. MCKITTRICK: What do you mean by that?

DR. HOLMES: It means that a considerable amount of peristaltic activity is going on in the small bowel.

DR. MCKITTRICK: Do the haustral-like formations suggest it?

DR. HOLMES: They are not haustral formations, of course; but they do look like them.

DR. MCKITTRICK: As I look at it, this looks almost like large bowel.

DR. HOLMES: That is so.

Another interesting thing is that there is no gas except in this loop.

DR. TRACY B. MALLORY: Can you be certain that it is small intestine, Dr. Holmes?

DR. HOLMES: Yes; I am reasonably certain. Of course one can make a mistake.

DR. MCKITTRICK: May I ask one more question? Are you certain enough so that you would advise a surgeon to do a laparotomy?

DR. HOLMES: Does it make any great difference whether the small or large bowel was obstructed?

DR. MCKITTRICK: It might make quite a lot of difference. If there was a question in the mind of the radiologist, the point that I want to bring out is, Would there have been any harm in putting barium into the rectum to make sure of the lesion?

DR. HOLMES: There would have been no harm. If it was large bowel, it could have been a volvulus; if small bowel, which I think it was, it was not necessarily a volvulus. The reason for a volvulus in the large bowel is that there was no gas anywhere else. If it was a loop of small bowel, I do not know how to explain the absence of gas in the rest of the bowel. The liver shadow is not increased in size, and I do not see the gall bladder or any evidence of gallstones.

I think that I shall have to admit that I do not see the soft-tissue shadows that are described. They may be there.

DR. MALLORY: In almost every history of this sort there is something that one cannot bring into the picture, but I think Dr. Hayden passed over the frankly bloody stool with slight comment.

DR. HAYDEN: Yes; I temporarily forgot about that. Of course, that did alter the picture just before the patient died.

DR. MCKITTRICK: Where do you think the thrombosis was?

DR. HAYDEN: Not being a peripheral vascular expert, I am in doubt whether she had thrombosis or embolism.

DR. MCKITTRICK: You would be in doubt if you were a peripheral vascular expert.

DR. HAYDEN: The history does not say much about the swelling of the legs—nothing about the degree of swelling. I might draw some conclusions from the location and appearance of the swelling, but since it involved both legs, I assume the vascular obstruction must have been around the bifurcation of the iliac arteries.

CLINICAL DIAGNOSIS

Occlusion of abdominal aorta, due to embolus, mural thrombus or dissecting aneurysm of aorta.

DR. HAYDEN'S DIAGNOSES

Thrombosis or embolism of iliac arteries.
Polycythemia.

ANATOMICAL DIAGNOSES

Gangrenous infarction of sigmoid (volvulus).
Hemoperitoneum, slight.

Ulceration of small bowel, postoperative.

Operative wound, fresh: lysis of adhesions about small bowel.

Operative wound, old: hysterectomy.

Arteriosclerosis, severe, aortic.

Thrombosis of abdominal aorta and both iliac arteries.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed, first, that the loop of small bowel that had been obstructed and had been returned to the abdomen as viable was still viable although distinctly discolored. There were small ulcers in the mucosa, but the bulk of the bowel wall was in good condition. On the other hand, inspection of the lower intestinal tract showed that the entire sigmoid was black and gangrenous. At the moment of examination it was not twisted upon itself. There were no thrombi in either the arteries or veins running to this loop of sigmoid so that the only explanation for this gangrene is that it was due to a volvulus. The other complicating feature, which unquestionably played a considerable role in producing death, was a thrombosis of the inferior aorta beginning just below the renal vessels and extending down the remainder of the aorta and far into both iliac arteries. The aorta was markedly sclerotic, with a great many shaggy thrombi overlying deep atheromatous ulcerations. We thought we could distinguish two ages of clot. There were many small clots adherent to the bases of the ulcers and then a much fresher and larger clot that completely occluded the aorta.

It is surprising, to me at least, how extensive ulcerative arteriosclerosis of the aorta can be at autopsy, and yet how seldom thrombi develop that are of significant size from the clinical point of view. However, I am reasonably sure this was a case in which the thrombus was locally formed from the atheromatous plaques.

The gall bladder was entirely negative despite the long history of apparent gall-bladder attacks.

DR. HOLMES: Were there any soft-tissue masses in the pelvis that could account for the shadows?

DR. MALLORY: No; unless they came from the sigmoid.

DR. HOLMES: What was the date of operation as compared with that of these films?

DR. MCKITTRICK: They were taken before operation. The dilated loops were the small bowel; I was trying to talk you out of it.

How often, Dr. Mallory, have you seen a thrombus that completely occludes the aorta? I am not referring to a thrombus which comes from higher up and causes an embolic occlusion.

DR. MALLORY: It is uncommon. I have seen it less than five times.

CASE 29142

PRESENTATION OF CASE

First admission. A forty-six-year-old housewife entered the hospital because of a persistent cough.

Approximately eight months before admission the patient developed a hacking cough and began to raise a small amount of sputum each morning that occasionally was blood tinged. There was slight dyspnea on exertion, but no cyanosis, palpitation, orthopnea, ankle edema, chest pain, fever, chills or night sweats, and she had gained 17 pounds during the six months preceding entry.

The family and past histories were noncontributory. There had been no contact with an open case of tuberculosis. A hysterectomy had been performed nine years before admission.

Physical examination disclosed a well-developed, obese, apprehensive woman who had a bothersome cough. The heart, lungs and abdomen were normal. A vaginal examination was essentially negative, and the fundus could not be felt.

The blood pressure was 130 systolic, 90 diastolic. The temperature was 98.6°F., the pulse 89, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,490,000, with a hemoglobin of 13.6 gm., and a white-cell count of 11,000, with 65 per cent neutrophils, 21 per cent lymphocytes, 10 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. The urine was acid in reaction and had a specific gravity of 1.012, and the sediment contained a rare red and white cell and 3 epithelial cells per high-power field. The blood Hinton test was negative. The sedimentation rate was 2, 5 and 9 mm. after thirty, forty-five and sixty minutes respectively. No acid-fast bacilli were seen in seven sputum examinations.

A chest roentgenogram disclosed a rounded, 4-cm., homogeneous area of increased density in the medial portion of the right infraclavicular area. There was no evidence of calcification or of cavity formation, and the right lung field was otherwise clear. Overlying the anterior end of the fourth left rib were two irregular areas of increased density. The remainder of the left lung field was clear. The heart and mediastinum were not remarkable, and there was no evidence of respiratory shift. Both sides of the diaphragm were smooth in outline and showed normal motion. A

review of films taken prior to entry showed much the same appearance except that the nodules in the left lung field were seen more clearly and appeared to be round rather than irregular. In the flat plate of the abdomen, the kidneys appeared normal in size, shape and position; no stones were seen. Intravenous dye was promptly excreted and outlined normal urinary passages.

Bronchoscopy on the second hospital day disclosed a normal trachea. The left bronchus was not entered, but on entering the right bronchus, the floor was displaced forward by extrinsic pressure. The orifice of the upper-lobe bronchus appeared angulated as though there were outside pressure on the superior angle where this bronchus met the main stem, thus displacing the opening downward and causing the superior lip to present sharply in the main-stem lumen. There was no visible growth, and nothing from which a biopsy could be taken. Sputum was obtained for acid-fast examination. The next day a pneumothorax was started in preparation for thoracoscopy. The patient was discharged unimproved on the ninth hospital day. X-ray films of the chest taken after the pneumothorax yielded no additional findings.

Second admission (one year later). The patient was readmitted for exploratory thoracostomy. Her symptoms had continued unchanged. An x-ray film of the chest taken a month after discharge revealed that the right lower lung had re-expanded, but that there was still a considerable quantity of air surrounding the collapsed right upper lobe. The mass in the right upper lobe had not changed except that it contained a questionably small area of diminished density suggestive of beginning cavity formation. The nodules in the left midlung field were not clearly visible and were approximately 1 cm. in diameter.

Physical examination was unchanged. The temperature, pulse and respirations were normal.

An x-ray film of the chest taken on the day of admission revealed that the "mass" in the right upper lobe had slightly increased in size and was approximately 7 by 7 by 6 cm. The cavity had also increased slightly. There was an area of atelectasis in the anterior portion of the base of the right upper lobe. The two small areas in the left lung field had not changed.

An operation was performed on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HELEN PITTMAN: I assume that the operation done nine years ago was at an outside hospital; hence, we do not know about the ovaries or why the operation was done.

The laboratory findings were essentially normal. It is not stated whether sputum taken at bronchoscopy was examined for tubercle bacilli or what the report was, and I do not know why they went ahead and did a thoracoscopy.

This patient was a forty-six-year-old woman in good health. Before the time of operation, she had had, for one year and eight months, a cough productive of small amounts of sputum, which was only occasionally, not regularly or daily, blood tinged. She had had slight dyspnea on exertion, had gained weight and had had a hysterectomy nine years before, for what reason or what was removed we do not know. It is the kind of problem that we are faced with frequently and it is a difficult one because we do not have much to go on. With each case of chest tumor we have to go through rather stereotyped processes of reasoning. First of all, we think of the possible diagnoses and the appropriate diagnostic procedures. If that does not give the answer we must come to the decision whether or not exploration should be done.

The most probable diagnosis is malignant tumor, either primary or secondary. If primary, we think first of primary carcinoma of the bronchus. There was some blood, but it was only occasional, and we have learned to realize that the bleeding which leads us to suspect carcinoma of the bronchus is the daily ooze, not the occasional blood streak. This patient had pressure on a bronchus that was enough to give an irritating cough and I think we can say that this small amount of bleeding was probably secondary to the irritation that comes from pressure and was not caused by bronchial ulceration. Other primary malignant tumors are extremely rare; these include sarcoma, lymphoma, dermoid cyst and teratoma.

May we see the x-ray films?

DR. GEORGE W. HOLMES: The first two films were taken before coming to this hospital. The lesion itself is distinctly lobulated. It varies somewhat in density, and within its substance are bright areas, which I think are bronchi but may be cavities. The heart and mediastinum are not displaced. There are no eroded ribs. The process is not adherent to the pleura because it was easily displaced after giving the pneumothorax. It is in the midchest—neither in front or in back, nor in the upper or the lower portion. In the opposite lung field there is a small irregular shadow that is visible in most of the plates and does not change appreciably in size during this period of time.

Certainly the change in the size of the lesion itself was not rapid. One must also consider the possibility that a bronchus was plugged and that this shadow was due to atelectatic lung around a

mass rather than to the actual mass. There was no fluid in the pleural space.

DR. PITTMAN: This does not look to me like metastatic disease in the chest, but we have to think of that and it is quite obvious that they were thinking of it when the patient was worked up on the first admission. There were two possible sources: the unknown pelvic situation nine years before, and the commoner one, hypernephroma which they obviously were considering. This to me is not at all the picture of what one usually sees with metastases from a hypernephroma. But when the flat plate and the pyelograms were made they probably had that in mind, and certainly it was the proper thing to do.

The next thing to consider in a chest of this sort is chronic infection, and the two infections that we see most commonly are tuberculosis and lung abscess. The history does not suggest infection. The patient had gained weight, had had fever, and had no anemia or leukocytosis—the white-cell count of 11,000 with 65 per cent neutrophils is essentially normal. She also had a low normal sedimentation rate. Repeated sputum examinations were negative for tubercle bacilli. We do not know whether acid-fast stains were done on material obtained through the bronchoscope. This is one of the cases in which tests with a series of dilutions of tuberculin might have been extremely important. In the presence of this lesion a negative test with a 1:1000 dilution of tuberculin would have enabled one to have ruled out tuberculosis.

Going back to the primary bronchial tumors, I must say that the sputum does not suggest such a tumor or ulceration into the bronchus, and the bronchoscopic examination was negative for a lesion of the bronchial wall. It did, however, show extrinsic pressure, so I think we can fairly safely reject from our minds a primary carcinoma of the bronchus.

Then one must consider benign tumors. This was an essentially asymptomatic mass, which did not affect the patient's health, and on bronchoscopic examination only revealed evidence of extrinsic pressure. Intrathoracic goiter and dermoid cyst are possibilities, but I feel perfectly sure that both can be discarded at this time.

On the patient's first admission she was put through the routine diagnostic procedures of x-ray study, blood work, bronchoscopy and pneumothorax. The last was done to learn whether it caused the lung to fall away from the pleura and hence made the lesion more clearly visible, and at the same time to show up the parietal pleural surface to see if it was smooth or showed nodules. At the time of discharge on the first admission the more serious diseases, for which one should in-

terfere, had been ruled out, and given a patient who was not sick it was reasonable to keep her under observation—to let her go home and to see how things went along.

That is apparently what was done. The x-ray taken one month after discharge shows that for at least a month she kept in contact; then she came back a year after the first admission still, we gather, in good health, with no significant change in the symptoms and with no fever. There are no reports of blood, urine and sputum examinations at that time, but I assume that they were still negative. Then comes the situation that must be frequently faced with these tumors. All the routine and reasonable diagnostic procedures have been carried out; the patient is in good health, but there is an increasing lesion. Is one justified in allowing it to ride any longer or must one explore and find out what is at the base of it? I think that is the really important point in this case. One can guess all day long about the diagnosis. All leads have been quite valueless, and while there is still time to do something, one should resort to exploration for purpose of diagnosis. I think that was probably the situation in this case.

One should have a preoperative diagnosis for a working basis. There are few clues to throw weight on any of the things that I have discussed. There is little evidence for infection, and a good deal of evidence against it. I am going to make a preoperative diagnosis of tuberculosis; possibly the mass was a tuberculoma or a large tubercle.

DR. TRACY B. MALLORY: The preoperative diagnosis was tuberculoma, Dr. Pittman.

DR. RICHARD SWEET: This was one of the most amazing cases we have had in a long time and I welcome the opportunity to find out what the pathologists found, because I have not heard. Because of the exigencies of the war, the patient had a complete change of doctors during a period of one and a half years. The surgeon who first saw her went to war, then the medical man went; finally the one who did the bronchoscopy entered the armed services. It was my impression that we did another bronchoscopy at the time of the second admission, but perhaps not. At any rate, the case was presented to me by her new physician for a decision whether we should do, as Dr. Pittman has said, an exploratory operation.

I was impressed by a number of clinical facts regarding this patient. First of all, after a year and a half she was in remarkably good condition and had no fever. This seemed to indicate that she did not have a wasting disease. From that standpoint, as you recall, Dr. Holmes mentioned a lesion in the left lung field, and it is my impression

that the surgeon who first reviewed her case believed that because of this lesion and the probability that she had tuberculosis it would be unwise to operate for fear of a flare-up on the left side. Since that time more lobectomies have been done for tuberculosis and perhaps we had more courage at the second admission than we had at the first. I was never convinced of the diagnosis of tuberculosis, although Dr. Mallory has said that the preoperative diagnosis was tuberculosis. My diagnosis was tuberculosis or cancer. I did not see how one could tell which it was. The reason I leaned a little toward cancer was that she had a persistently bloody sputum. It is unfortunate that Dr. Pittman was not given that information in the record. The patient was worried about herself because of this blood-tinged sputum almost every day. That to me usually means carcinoma. On the other hand the history was a long one. Patients with carcinoma of the lung, even of only a few months' duration, are usually in poor physical condition, but this woman was in good shape. So although we really had no accurate information concerning the diagnosis, I leaned toward carcinoma, as did the medical man who had her in charge, as well as some of the others who saw her, including one physician whose knowledge of tuberculosis is extensive.

At operation the condition was still puzzling. The lesion involved the upper lobe. It was not adherent. As soon as air was introduced into the chest it fell away from the chest wall. It had a round contour like that of a swollen liver. The surface was depressed, and there was a milky film over its surface. As I felt of it, it had a rubbery consistence; it was not hard and firm like a carcinoma. I could not tell what it was. There were no enlarged lymph nodes at the hilum, which is consistent with the diagnosis of tuberculosis. In the majority of carcinoma cases, on the other hand, the nodes are involved. Removal of the lobe was easy. Her convalescence was as smooth and uneventful as any I have ever seen, and that to me is circumstantial evidence in favor of the diagnosis of carcinoma.

DR. MALLORY: Do you care to say any more, Dr. Pittman?

DR. PITTMAN: I should feel, as Dr. Sweet did, that if the patient was having daily bleeding one would have to consider carcinoma much more seriously than I considered it, although it certainly is unusual to have a bronchoscopy merely showing evidence of extrinsic pressure.

DR. SWEET: I do not understand the bronchoscopic report. They say there was evidence of pressure on the trachea or bronchi, but at the time of operation there was none whatever.

DR. MALLORY: Dr. Robbins, have you any comments?

DR. LAWRENCE ROBBINS: No; my diagnosis was tuberculoma from the way the lesion had progressed.

DR. HOLMES: The x-ray evidence is in favor of tuberculoma.

CLINICAL DIAGNOSIS

Carcinoma of lung?

Tuberculoma?

DR. PITTMAN'S DIAGNOSIS

Tuberculoma.

ANATOMICAL DIAGNOSIS

Metastatic papillary cystadenocarcinoma of ovary.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Castleman, who schedules these conferences, sometimes plays a trick on me. When we have a particularly difficult specimen over which I delay about committing myself, he occasionally puts it on for clinicopathological conference without warning and I have to make up my mind. I think that is the reason this case was scheduled.

I am not a bit sure what the diagnosis is. About four fifths of the right upper lobe was replaced by a rather firm, but not extremely hard, tumor. Grossly it looked like tumor and certainly was not tuberculosis, but it was peculiar in several respects. There were four small cystic cavities within the solid tumor that did not seem to be bronchi, and each of them contained mucoid material. They seemed to be part of the tumor.

The microscopic sections present a very unusual appearance. The architecture of the lung is perfectly preserved. The bronchi are lined with perfectly normal ciliated epithelium, and the great majority of the alveoli are lined with extremely high columnar epithelium that is obviously secreting mucus. This epithelium projects into the lumens of the alveoli in papillary masses, and there is no destruction of the alveolar walls that can be clearly outlined by elastic-tissue stains. The appearance of the cells, the papillary character and the mucoid secretion are all similar to the findings in papillary adenocarcinoma of the ovary. This woman had had a hysterectomy nine years previously and we have not yet succeeded in checking up on the findings of that operation. It is conceivable that this represents metastasis from an ovarian tumor. On the other hand this would

be an extraordinary course for a malignant ovarian cyst. They almost always extend first through the wall of the cyst to the peritoneum, then produce widespread peritoneal implantations followed by ascites, and distant metastases are quite uncommon. Metastasis from a papillary pseudomucinous ovarian cyst must remain a possibility. It is still a question whether the masses in the other lung were likewise metastatic, and it is difficult to explain why one should grow and two others remain the same size.

The other possibility is that this was a primary tumor of the lung, and in favor of that I have seen just one other case which to my recollection is exactly similar in growth and histologic appearance. That case occurred in a man so that ovarian cyst was out of the question; moreover we had an autopsy and found no tumor outside the lung. However, the thyroid, a frequent source of papillary adenocarcinoma, was not examined. If the tumor was primary it seems to be essentially a carcinoma of the alveoli with no demonstrable connection with any bronchus, and there is so little evidence that alveolar epithelium actually exists that one hesitates to make such a diagnosis. I have to leave the question open.

DR. SWEET: From the clinical picture, I should accept the diagnosis of primary tumor of the lung much more readily than anything else. I have never seen any other case exactly like this one.

DR. MALLORY: It is very unusual for a tumor to invade an entire lobe of the lung, growing simply along the surfaces of the alveoli and producing no destruction of the lung tissue, but I have occasionally seen similar pictures before.

DR. HOLMES: What do you think of the lesions in the other lung? Were they just a red herring?

DR. SWEET: They have not changed over a period of observation. Everyone has been looking at them and expecting them to clear up. Those who vote for tuberculosis use these lesions as evidence for tuberculosis. My opinion was purely clinical and was not based on the x-ray findings.

Addendum. Between presentation of this case at conference and publication it was discovered that a papillary pseudomucinous cyst of the ovary was removed at the time of the hysterectomy. Dr. Arthur T. Hertig, of the Free Hospital for Women, Brookline, kindly loaned me a microscopic section for comparison. The character of the two tumors is identical, so I believe the major pulmonary lesion was unquestionably metastatic, and my guess is that the smaller lesions in the opposite lung must be also.—Tracy B. Mallory.

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ABSENTEEISM IN INDUSTRY

IN the beehive the individual is recognized either as a worker or a drone, and is promptly and appropriately dealt with on that basis. Thus the hive is not plagued by absenteeism in any form. Fortunately or unfortunately, human beings have not evolved the social insight of the bees, and they must consequently cope with this distressing quirk of human behavior whenever and wherever groups of persons gather and attempt to correlate their efforts. Absenteeism has long been recognized as a phenomenon of school life, college life and adult life. One would like to believe that it is progressively outgrown and appears less frequently in

adolescence and maturity, but such is probably not the case.

One might like to assume that human beings could be separated, like the bees, into groups that could be defined and labeled as workers or drones. Although there are undoubtedly many human beings in both these categories, there also are many who are subtly placed in between such groups. As one visualizes the various shades of people represented among his acquaintances he discerns certain behavioristic patterns that would bear heavily on the incidence of absenteeism in their industrial employment. There are the hard workers, those who—sick or sore—report for duty punctually, and, so long as they can stand on their feet, deliver their full measure of effort. Next there are those who absent themselves only when they are definitely sick and who return at the earliest possible moment to steady employment—the “conscientious” people. Next are those who are “spleeny,” who make the most of whatever illness they have and manage to make a good deal of some illnesses that they do not have. Then come the willful absentees—those who cannot recognize either our national perils or our national opportunities as their own. They may be motivated by excessive selfishness or deficient intellect, and they rationalize their absenteeism by all sorts of sophistries. For example, one is quoted as saying, “They won’t give me a vacation, so I’ve got to take it myself.” Many are undisciplined, unaccustomed and frankly unsuited to the work they are attempting to accomplish in industry, including those who are laboring in factories for the first time and those who are desperately trying to make themselves useful in fields to which they have not been and never will be naturally adapted. Lastly come those on whom the world has bestowed such adjectives as “lazy,” “incompetent” and “inadequate”—the people who in normal times are unable to obtain or hold a job of any sort.

Because sickness is the only indisputable status with which to explain most absenteeism, the physi-

cian's association with all these factors is close and decisive. Doctors have long been called on to certify that overwrought students are nervously or otherwise ill at the moment they face a critical examination. The cutting of classes for hours and sometimes for days preceding an examination has been frequently observed in school and college. There is a sort of epidemiology to this kind of behavior, academic outbreaks of which can often be satisfactorily analyzed. Industrial absenteeism is not so readily studied or understood, however, because the basic groups concerned have fewer common denominators than have the semidisciplined student bodies. The rapid labor turnovers of today also mitigate against an understanding of the underlying mechanisms. Nevertheless, alarm is being expressed over the effect that absenteeism is already having on war production, and an effort to deal sternly with it may come at any time. When it does appear, the physician is apt to find himself in the vortex of many a little cyclone.

GOOD HUNTING

AN entertaining intellectual exercise is provided if we try, occasionally, — perhaps idly, — to formulate for ourselves the real meaning and value of our culture and our civilization. That they have had, and have, real value for us is beyond question, for they have represented standards that we are apparently willing to make great sacrifices to preserve.

We were wrong, however, in assuming too readily that the environmental influences of our culture had made somatic changes in us; that our exposure to knowledge, ethics and brotherly love had made some vital change in our genes, transforming us into a morally superior race, forever and ever, amen. New species are developed, we know, as the descendants of Mendelian sports, but they do not arise because great grandfather had a good teacher at Latin School. They come because of internal explosions, not because of concussions at the periphery of the organism.

Most interesting, in support of this thesis, is the ease with which, from clerk to clergyman, from pharmacist to farmer, we again become the killer. We thought of battle murder and sudden death as something belonging to a relatively forgotten era, at least a generation away, or to a locality geographically remote, and certainly something relished by people less refined than ourselves. Then come the threat and the blow, and the discipline of our culture is superseded by the law of the claw and the fang. We want our enemies to be killed, mercilessly and in great numbers, and we want photographic evidence of the killing, with our breakfast.

It is an amazing metamorphosis — a strange and rapid indoctrination, albeit a necessary one. A few short years ago the paths of righteousness were the paths of peace. The popgun, that youthful symbol of violence, was hidden away; the smitten yearling was instructed to turn the other downy cheek; we were on the verge of spiritual vegetarianism. And now, of a sudden, the toy cannon has come down from the attic, lead soldiers again march and countermarch across the playroom floor, while the eyes of its occupant sparkle with joy at the news of fifteen thousand Nipponese adventurers entering their own peculiar eternity beneath the waters of the Pacific. Emotionally we are again meat eaters, as we are in practice, when we can get the meat.

Our culture and our intellectual way of life have meaning and value for us, but not because they have changed our fiber or altered our capacity. It is because of the discipline of thought and action that they have given for our support, and the code of ethics that they have furnished for our guidance.

MEDICAL EPONYM

THOMSEN'S DISEASE

The Schleswig practitioner who described this symptom complex, Asmus Julius Thomsen (1815-1896), of Kappeln, was himself a victim of the disease, which had been graphically described by Charles Bell in his book *The Nervous System*. In Thomsen's paper, "Tonische Krämpfe in willkürlich beweglichen Muskeln in Folge von erblicher psychischer Disposition (Ataxia Muscu-

laris ?) [Tonic Spasm of the Voluntary Muscles as the Result of a Hereditary Psychic Predisposition (Ataxia muscularis ?)]," which appeared in *Archiv für Psychiatrie und Nervenkrankheiten* (6:702-718, 1876), he quotes Bell's description. A portion of the translation follows:

Certainly the most essential feature of the affection is a weakness in the influence of the will on the organs of voluntary motion, which manifests itself in all the muscles, sporadically in any one, sometimes in all of them, but chiefly in those of the extremities, especially the legs. These members are not so subject to the will as they should be, and at times give way entirely. . . . The phenomenon is frequently most strikingly apparent in the gait, which, when the tendency to these cramps is present, quite resembles that of a drunken man until the spasm relaxes. The principal exciting cause is a psychic one—the fear of the curse of making one's self ridiculous.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON INDUSTRIAL HEALTH

The program for the Institute on Industrial Health, to be held at the Harvard Club of Boston, on April 24, under the auspices of the Committee on Industrial Health, is as follows:

- 9:30 Methods Used in Establishing a Diagnosis of Industrial Poisoning. Dr. Joseph C. Aub.
- 10:00 The Late Effects of Craniocerebral Trauma: A consideration of the criteria necessary to evaluate the possible causes. Dr. Donald Munro.
- 10:30 Medical Aspects of Absenteeism in Industry. Dr. Louis R. Daniels. Discussion by Dr. Daniel L. Lynch and Dr. A. W. Reggio.
- 11:15 Medical Causes for Rejection in Selective Service. Lt. Colonel Lewis S. McQuade.
Neuropsychiatric Causes for Rejection in Selective Service. Dr. Harry C. Solomon.
Discussion.
- 12:30 LUNCHEON (Guest speaker: Dr. Alice Hamilton).
- 2:15 Present Status of Relation of Heart Disease to Industry. Dr. Paul D. White.
- 2:45 Epidemic Keratoconjunctivitis. Dr. Irving R. Tabershaw.
- 3:15 Opportunities for the Prevention and the Treatment of Diabetes in Industry. Dr. Elliott P. Joslin.
The Treatment of Trauma in Diabetic Employees. Dr. Leland S. McKittrick.
Industrial Hazards for Diabetic Employees. Dr. William A. Bishop.
- 4:15 The Problems of Women in Industry. Dr. Thomas L. Shipman.
Discussion.

DWIGHT O'HARA, *Chairman*

SOCIETY HEADQUARTERS

Since the Boston Medical Library is now provided with adequate heating facilities, the headquarters of the Society and the office of the *Journal* have resumed their usual time schedule—nine until noon on Saturdays and nine until five on other days of the week.

Incidentally, the Library will be open from nine until nine on Mondays and Thursdays, from nine until five on Tuesdays, Wednesdays and Fridays and from nine until one on Saturdays.

TREASURER'S REPORT

REFUND DISTRIBUTIONS

The treasurer of the Massachusetts Medical Society makes the following report regarding the refunds to the district societies for 1943:

The Council voted to distribute the sum of \$4000 to district societies. The total number of payments of annual dues received by the Treasurer by March 1, to be counted for the refund, was 3466. Therefore the refund to the district societies for each paid fellow is \$1.154.

The following table gives the number of payments as of March 1, and the refund to each district as of April 1:

DISTRICT	NUMBER REPORTED	
	PAID	REFUND
Barnstable	31	\$ 35.78
Berkshire	94	108.49
Bristol North	51	58.87
Bristol South	157	181.20
Essex North	137	158.11
Essex South	191	220.43
Franklin	34	39.25
Hampden	214	246.98
Hampshire	47	54.25
Middlesex East	93	107.33
Middlesex North	84	96.95
Middlesex South	698	805.50
Norfolk	600	692.41
Norfolk South	103	118.87
Plymouth	104	120.03
Suffolk	466	537.78
Worcester	289	333.52
Worcester North	73	84.25
Totals	3466	\$4000.00

In 1942, for comparison, the total number of payments for the refund was 4023.

ELIOT HUBBARD, JR.
Treasurer pro tempore

COMMITTEE ON MATERNAL WELFARE

BREACH DELIVERY OBSTETRIC CONSIDERATIONS

The two previous reports in this column have demonstrated and discussed the neurologic hazards of breech delivery to a baby. In addition, the baby may have a fractured femur, humerus or clavicle; such accidents, however, are minor, because the fractures heal with minimal residual deformity and rarely, if ever, cause disability. The added risk to the mother also deserves consideration.

Third degree lacerations are much more frequent in breech deliveries, particularly in primiparas. On the other hand, there should be no greater tear of the cervix in breech extraction than in vertex delivery, because the delivery should never be attempted until full dilatation has been accomplished. The same hazards observed in breech delivery are associated with internal podalic version.

In the eighth edition of Williams's textbook on obstetrics, it is estimated that 311 per cent of all presentations are breech. According to statistics, the fetal mortality of breech presentation is largely dependent on the presence or absence of complications. Cases complicated by syphilis, toxemia, hydramnios, placenta previa, premature separation of the placenta, and prolapse of the cord showed a fetal mortality of 21.2 per cent in a study made by Grethals at the Boston Lying-in Hospital; however, in full term uncomplicated pregnancies the mortality was only 6.9 per cent. These figures emphasize the seriousness of breech delivery and the need for giving special attention to all such cases.

Because it is recognized that the vertex presentation carries with it much less risk than the breech presentation, the maneuver of external version, even under an anesthetic, is prescribed in some clinics. This is often simple, particularly in multiparas with relaxed abdominal walls. In primiparas with good sized babies, however, it is difficult or even impossible. Experience has proved that when it is difficult to turn the baby externally, and anesthesia has been resorted to, too much force may be applied, with the result that interference with the cord, partial separation of the placenta or premature labor occurs. Because of these possibilities, if external version cannot be readily accomplished, the use of an anesthetic had best not be made routine.

The problem of the breech in an elderly primipara, whose baby, because of her age, assumes great importance, has led to the adoption of cesarean section. This certainly is not always justifiable and should depend on the size of the baby and whether or not the membranes have ruptured prematurely. If the baby is large and the pelvis is small, the advisability of cesarean section should be

considered. External version should always be attempted, but as already stated, the maneuver should not be carried out as a routine procedure under anesthesia. In young primiparas, premature rupture of the membranes, with the breech remaining high, again raises the question of cesarean section. Experience, x ray studies of the pelvis and the character of the cervix should determine the need of operation. To say that cesarean section is an unnecessary operation on all breech presentations is just as foolish as to say that all such babies should be delivered by cesarean section. Cesarean section has its place, but each case must be intelligently evaluated.

External version and cesarean section have been employed to lower the mortality and morbidity in heretofore attendant on breech deliveries. It should be borne in mind that some breech deliveries are easy and that some, even in the hands of the most expert, are extremely difficult. The obstetric details of the case reported in the *Journal* four weeks ago are lacking, and it is consequently unfair to be too critical. However, unless there were unusual complications, it seems as though the injuries to the baby, who weighed 6 pounds, 2 ounces, can be attributed only to inexperienced operating. The diagnosis of a breech presentation late in pregnancy should stimulate the question, Will the baby come through this pelvis? If the pelvis is large and the baby seems small, then no x ray studies should be necessary. In borderline cases x ray films of the pelvis should be obtained, then, with all the facts at hand, it should be decided whether the baby can or cannot be delivered through the pelvis with safety. If an affirmative decision has been arrived at, the mother should be allowed to go into labor, and to reach full dilatation before any interference is resorted to. The membranes should never be ruptured. There should be no set time at which operative interference is attempted, because frequently such cases need no interference. The mothers have a normal labor, and to say they should be delivered when fully dilated is unintelligent and often leads to unnecessary meddling.

The double footling is relatively simple to deliver. In the frank breech, however, the legs sometimes become flexed on the abdomen and their delivery is difficult. In an attempt to deliver the flexed legs the femur may be fractured.

In breech or footling deliveries, traction on the baby's extremities is used, and all such traction must be gentle. No breech delivery should be accomplished with any specific idea of haste. When the scapulas appear at the vulva, the arms usually extend themselves downward and are born without assistance if the trunk is rotated from one side to the other. This rotation must be gentle

but not forceful. One of the most important considerations in the conduct of breech labor is to have a trained anesthetist who understands intelligent suprapubic pressure.

The delivery of the breech is simplified by a median or mediolateral episiotomy. Its purpose is to avoid tearing of the sphincter and to allow more room in which to work. In former days, breech deliveries, particularly in primiparas, were looked on as extremely hazardous from the standpoint of the mother because of the technic employed in the delivery of the arms. The operator inserted his hand into the vagina when the scapulas appeared; he hooked his fingers in the elbow of the posterior arm, and the forearm was thus extended downward over the abdomen. The baby's body was then rotated so that the anterior arm became posterior, and this arm in turn was extended by the operator's fingers in the elbow. This maneuver frequently resulted in third-degree lacerations. Episiotomy plus rotation of the trunk usually enables the arms to extend themselves downward and thus lessens this hazard materially. When the arms are delivered, the operator puts his finger into the baby's mouth to assist flexion of the head. He must never pull downward on the head, and must never stretch the baby. Unless there is undue disproportion between the baby and the pelvis, suprapubic pressure, aided by the operator's hand in the baby's mouth, almost always promotes delivery of the head through the pelvis. From the time the buttocks appear, the patient should be under full anesthesia so that suprapubic pressure may be accomplished easily. If there be any difficulty with the birth of the head by suprapubic pressure, the Piper forceps should be immediately employed. This instrument should always be boiled with the kit so that it is immediately available.

All statistics of a large number of cases are based on the work of many men. It must, of course, be true that in the hands of trained specialists, breech mortality and morbidity are lower than they are in the practices of those who deliver only an occasional case. However, a careful evaluation of each case before labor starts or at its onset and more gentleness and less haste in the actual delivery will undoubtedly lead to better results.

DEATHS

JEWETT—**HOWARD W. JEWETT, M.D.**, of Lowell, died March 18. He was in his sixty-fourth year.

Dr. Jewett was born in Haverhill. He received his degree from Hahnemann College in Philadelphia in 1905 and interned at the Millard Fillmore Hospital, Buffalo, New York. At the time of his death, he was the senior member of the medical staff at the Lowell

General Hospital. He was a member of the Massachusetts Medical Society and the American Medical Association.

His wife and a brother survive him.

MILLER—**GEORGE F. MILLER, M.D.**, of Belfast, Maine, died March 22. He was in his sixty-eighth year.

Dr. Miller graduated from Tufts College Medical School in 1908. He was a member of the Massachusetts Medical Society and the American Medical Association.

RICE—**GEORGE B. RICE, M.D.**, of Boston, died March 28. He was in his eighty-fifth year.

Dr. Rice attended the University of Michigan, where he received his degree. He was a member of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons. At the time of his death he was consultant in the Nose and Throat Service at the Massachusetts Memorial Hospitals.

His widow and three sons survive him.

RESOLUTION ON DEATH OF PHILIP ROCHE DWYER

The Boston City Hospital mourns the death of Dr. Philip Roche Dwyer, a visiting surgeon on the Ear, Nose and Throat Service. He died in Salem, Massachusetts, on February 28, 1943, at the age of forty-nine.

His parents, the late Philip and Bridget Dwyer, were Beverly residents, and he was born there on February 3, 1894. After attending the local schools he entered Boston College and received his degree in 1916. He graduated from the Harvard Medical School in 1920.

He interned at the Boston City Hospital, where he graduated on November 3, 1921, from the Eye, Ear, Nose and Throat Service. He was immediately appointed a staff member on that service. He was affiliated as a visiting surgeon at the Salem, J. B. Thomas, Peabody and Danvers State hospitals. Dr. Dwyer had practiced his chosen specialty in Salem for the past twenty-three years. He was a member of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, Elizabeth M. (Prendergast) Dwyer, a daughter, Elizabeth, and a sister, Miss Mary Dwyer, all of Salem.

Dr. Dwyer was of sterling character, and although enduring many physical handicaps, he was never heard to complain. An able diagnostician, his technical skill was of high order. His engaging smile was one of his outstanding characteristics; his spontaneous wit portrayed his buoyant spirit. He was "our kind" of a man; his life was an inspiration to all.

He was operated on for a ruptured diverticulum at the Salem Hospital. A scheduled blackout took place during his convalescence there. At that time

many staff friends came to his room to joke and discuss the topics of the day. After their departure he asked to be turned on his side—and the end came, painlessly and mercifully, and the valiant spirit of Philip Dwyer passed on. But there was a "blackout" during his life for he denied the sunshine of his smile to none, and we know that God's eternal glow is his forever.

BE IT RESOLVED, that in the death of Philip Roche Dwyer the staff of the Boston City Hospital has lost one of its most learned and beloved members; BE IT RESOLVED, that the staff of the Boston City Hospital extends its most sincere sympathy to his family; and

BE IT FURTHER RESOLVED, that these recommendations be placed on the records of the Boston City Hospital and that the secretary be directed to send copy to the family of Dr. Dwyer and a copy to the *New England Journal of Medicine*.

WILLIAM P. BOARDMAN, *Secretary*
Executive Committee, Senior Staff
Boston City Hospital

LABOR ACTIVITIES

INDUSTRIAL MEDICINE

PRECAUTIONARY MEASURES FOR WORKERS HANDLING CHLORINATED NAPHTHALENES AND DIPHENYL COMPOUNDS

In connection with the recent outbreaks of dermatitis and systemic injuries resulting from the use of chlorinated naphthalenes and diphenyl compounds in the State of New York, Dr. Leonard Greenburg, director of the Division of Industrial Hygiene, New York State Department of Labor, has suggested that precautionary measures covering the following points be formulated in co-operation with the manufacturers of these compounds for the protection of workers handling these materials:

- (1) Recognition of an agreement on toxicity of compound.
- (2) Warning to users—agreement to provide all users with notice.
- (3) Warning to middle men who sell the material in small lots to users.
- (4) Provision by the companies of a statement covering measures for protection.
- (5) Agreement by employers to provide pertinent state authority with a list of users and also a list of applications or processes in which the material is used. (This list of users should be kept up to date.)

An evaluation of the potential dangers of these materials is desirable. Hence it has been requested that reports on the incidence of such injuries in different states be sent to Dr. J. G. Townsend, chief of the Division of Industrial Hygiene, National Institute of Health. The following information is to be included in these reports:

- (1) The number of cases of dermatitis or systemic poisoning that have occurred in each state.

- (2) The duration of the disease (time lost from work).

- (3) The industry and specific occupation in which these cases occurred.

- (4) The name of the material that was the causative agent.

It is planned to call a meeting of representatives of the five manufacturers of these materials with the Chemical Products Agreements Committee appointed by the Surgeon General.

With this procedure it is hoped that the hazards resulting from the handling of these materials can be adequately controlled.—Reprinted from *Industrial Hygiene* (March, 1943), a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

BOOK REVIEWS

Biological Symposia: A series of volumes devoted to current symposia in the field of biology. Edited by Jaques Cattell, Ph.D. Vol. VII. *Visual Mechanisms.* Edited by Heinrich Klüver, Ph.D. 8", cloth, 322 pp., with 4 tables and 83 illustrations. Lancaster, Pennsylvania: The Jaques Cattell Press, 1942. \$3.25.

To celebrate the fiftieth anniversary of the University of Chicago in 1941, a series of symposiums in biologic sciences was arranged dealing with new frontiers in education and in research. Not the least interesting of these was the seventh, held in September, 1941, in which visual mechanisms were discussed by authorities from the points of view of anatomy, biophysics, biochemistry, physiology and psychology. The scope of the presentations is best shown by a list of the titles and authors: "Energy Relations in Vision" by Dr. Selig Hecht; "The Photochemistry of Visual Purple" by Dr. A. C. Krause; "Visual Systems and the Vitamins A" by Dr. George Wald; "Anoxia in Relation to the Visual System" by Dr. E. Gellhorn; "Visual Sensation and Its Dependence on the Neurophysiology of the Optic Pathway" by Dr. S. H. Bartley; "Alpha Waves in Relation to Structures Involved in Vision" by Dr. T. J. Case; "Recent Evidence for Neural Mechanisms in Vision Leading to a General Theory of Sensory Acuity" by Drs. W. H. Marshall and S. A. Talbot; "The Functional Organization of the Occipital Lobe" by Drs. G. von Bonin, H. W. Garol and W. S. McCulloch; "Anatomy of the Retina" by Dr. S. L. Polyak; "The Visual Cells and Their History" by Dr. G. L. Walls; "Functional Significance of the Geniculostriate System" by Dr. H. Klüver; "The Problem of Cerebral Organization in Vision" by Dr. K. S. Lashley.

Every researcher who wishes to keep abreast of the advancing frontiers in visual anatomy, physiology and psychology, and every alert practitioner of ophthalmology who wishes to be more discerning in his field would do well to add this important volume to his library.

Physicians' Reference Book of Emergency Medical Service. A compilation. 8", paper, 268 pp., with 15 illustrations and 8 tables. New York: E. R. Squibb and Sons, 1942. Complimentary.

This compact volume covering the Emergency Medical Service is divided into three sections. The first deals with precautionary measures, the second with hospital services, and the third with the management of casualties. The handbook mainly contains abstracts from articles writ-

ten by experts on each subject. The material is of recent publication, and many of the articles are from British sources.

In the first section, much sound advice is given concerning the immediate care of the injured, and the extreme importance of getting casualties to the hospital as quickly as possible is stressed. Moreover, fixation of the casualty to the stretcher in such a way that he may be brought to the hospital with as little danger as possible is emphasized. A number of different types of stretchers are depicted, and the correct maneuvers for the immobilization of various types of injury are illustrated.

In the second section, twenty-eight pages are devoted to the modern treatment of burns. The triple-dye, tannic acid and silver nitrate methods, together with saline treatments and different methods of transfusion, are given careful consideration. The general treatment of shock, the theories concerning its causes and the importance of transfusion are taken up in a simple and direct manner. Due attention is given to the use of sulfonamide drugs orally, intravenously and locally. The last part of this section concerns war-gas injuries, a valuable chart describing the different gases and their effects. Rules for decontamination of road surfaces, of buildings and household articles and of vehicles are given. The differential diagnosis of the effects of the various gases is considered, including those affecting the respiratory system, the eyes and the skin.

The book is small but valuable. The descriptions of the different types of emergency medical service are given with remarkable clearness, and the material collected for the volume was judiciously chosen. Every physician should have a copy of this volume.

The Medical Applications of the Short Wave Current. By William Bierman, M.D. With a chapter on physical and technical aspects by Myron M. Schwarzschild, M.A. Second edition. 8°, cloth, 344 pp., with 87 illustrations. Baltimore: The Williams and Wilkins Company, 1942. \$5.00.

In the introduction to the present edition the author states that it is estimated that approximately fifty thousand short-wave-current machines are in use in physicians' offices and hospitals in the United States. It requires a good deal of optimism to believe that this great volume of apparatus is employed by people who are well versed in the underlying theory of these currents, the construction of the machines that produce them, their effects on the tissues of the human body, the technics of application and, last but not least, the necessary precautions that must be taken to avoid injuries in the form of deep-seated burns. Such valuable information was contained in the first edition of this text and has been sifted, rearranged and greatly enriched in the second edition.

It is to be regretted that the authors saw fit to ration the chapter on physics, reducing it to about a third of its original size. This section was one of the highlights in the first edition and, in the opinion of the reviewer, should have been revised rather than drastically curtailed. The market is not overburdened with texts whose authors have taken pains to present this aspect of the subject so thoroughly as was done by Schwarzschild in the first edition. On the other hand, the inclusion of a twenty-four-page chapter on fever therapy is a distinct addition. Its importance looms high when one takes into consideration the fact that Dr. Bierman's meritorious contributions

to this subject have gained for him wide recognition. Furthermore, the illustrations and bibliography have been improved.

This is a praiseworthy treatise on an extensively practiced but insufficiently illuminated aspect of physical therapy.

The Electrocardiogram and X-Ray Configuration of the Heart. By Arthur M. Master, M.D. Second edition, enlarged and thoroughly revised. 4°, cloth, 404 pp., with 163 illustrations. Philadelphia: Lea and Febiger, 1942. \$7.50.

The new edition of Master's excellent book should be required reading for every serious student of electrocardiography. It is not intended to take the place of a textbook of electrocardiography, but it does fill some important gaps that cannot be considered fully in such a book. Interpretation of the electrocardiogram without full knowledge of all the possible extraneous factors that may have influenced it is dangerous and may be misleading. Dr. Master's book shows clearly the many variations incident to age, body build, pulmonary disease, rotation of the heart, acute infections and enlargement of the various chambers of the heart, as well as the more commonly recognized patterns associated with intrinsic myocardial damage. The volume also constitutes a good complete x-ray monograph of the heart. This edition contains considerable new material, including the Diard method of contrast visualization of the cardiac chambers.

Dermatologic Therapy in General Practice. By Marion B. Sulzberger, M.D. Second edition. 8°, cloth, 632 pp., with 67 illustrations and 25 tables. Chicago: The Year Book Publishers, Incorporated, 1942. \$5.00.

This book is valuable not only as a handbook of therapy for the general practitioner but also as a ready reference for the specialist. The outlines of treatment of the various cutaneous diseases are easily understood and practical. It reveals the pitfalls, and emphasizes not only what to do but what not to do. There are over two hundred useful prescriptions. New methods of therapy, such as the use of the sulfonamide group, the treatment of burns and the technic of massive-dose therapy of syphilis are wisely discussed. This book is worth buying.

The Surgery of Pancreatic Tumors. By Alexander Brunschwig, M.S., M.D. Illustrated by Gladys McHugh. 4°, cloth, 421 pp., with 123 illustrations and 1 color plate. St. Louis: The C. V. Mosby Company, 1942. \$7.50.

This excellent treatise on the surgery of pancreatic tumors is recommended to everyone practicing surgery. Covering as it does the historical aspects, anatomy, embryology, physiology, experimental surgery and various other pancreatic problems, it makes readily available all the necessary material, to bring the surgeon up-to-date on this subject. It describes modern technics for the removal of all types of pancreatic tumors and presents discussions of the diagnoses of these conditions. In the reviewer's opinion, there is no comparable work in the literature on this subject. The text is well written in simple language, and is logically arranged. The illustrations are adequate, ample and easily understood.

(Notices on page x)

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RESTING-PULSE AND BLOOD PRESSURE VALUES IN RELATION TO PHYSICAL FITNESS IN YOUNG MEN*

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IT IS customary to assume that the resting pulse of a normal adult man is about 70 beats per minute. The common belief is that when the resting pulse deviates much from this usual value, the heart is abnormal or there is functional disturbance of the circulatory mechanism associated with some medical condition such as infection or hyperthyroidism. Exception is made when one is dealing with well trained athletes, whose resting pulse is usually lower than that of less trained or untrained persons. Resting pulses as low as 40 beats or even less have been observed in men who were accustomed to long and hard physical performances and who had been under fairly continuous training for periods of years.^{1,2} A high resting pulse is more often regarded as a pathologic sign, and pulses above 100 are considered so abnormal that, according to many physicians, a man whose cardiac rate remains persistently over 100 should be discarded from combat service in the Army or Navy. Cases have been called to our attention of outstanding athletes who have been rejected by examining boards because of high resting pulse.

Is the resting pulse an indication of the state of a man's physical fitness for hard muscular work? Data obtained in the course of general research in the Grant Study since 1938 help to clarify the problem. These data reveal a wide variability in normal young men that has not been sufficiently recognized.

The basis for this study was a series of measurements made on 265 college students selected without reference to athletic ability or physical fitness. For comparison, measurements were also made on a group of college athletes. The ages ranged from seventeen to twenty-two years. All the subjects

had been previously declared normal after careful medical examination.

PULSE AND BLOOD PRESSURE AT REST IN NORMAL YOUNG MEN

The basal pulse was counted in the morning, the subject being in the fasting state, after lying down for one hour for a basal metabolism determination. The recumbent, sitting and standing pulse and blood pressure were taken during the course of the medical examination. The pulse and blood pressure were taken again while the subject was sitting for a period of at least ten minutes before a test on the treadmill. In this case the heart rate was recorded continuously by means of a Guillemin cardiograph, so that the subject did not know when his pulse was taken. The lowest reading obtained during this rest period was designated as the "sitting pulse before the treadmill."

Table 1 summarizes the findings on the college students. It is seen that under conditions of a routine and strictly private medical examination, performed by a physician who was known beforehand by the subjects, 6 men had a sitting pulse persistently above 100, and 12 men out of 253 had a systolic blood pressure persistently above 140 mm. It is also seen that the systolic blood pressure remained practically the same whether measured during the medical examination or before an experiment on the treadmill. On the other hand, the sitting pulse was definitely higher when taken before the treadmill test than during the medical examination.

PULSE AND BLOOD PRESSURE IN RELATION TO PHYSICAL FITNESS

An extensive study was made on 129 students and 18 varsity oarsmen in training. Their capacity to perform hard muscular work was measured. It included the following determinations: duration

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of a run on a motor-driven treadmill at 7 miles per hour on an 8.6 per cent grade; blood pressure before and after work; pulmonary ventilation and oxygen consumption during the run; heart rate before, during and after work; and blood sugar

as well as those between standing and lying pulses, also showed no relation to capacity to perform hard work. On the other hand, a close relation was found between performance capacity and rate of deceleration of the heart after work on the

TABLE 1. *Averages and Extremes of Pulse and Systolic Blood Pressure in Normal Young Men at Rest and before Muscular Exercise.*

MEASUREMENT	NO. OF CASES	AVERAGE	EXTREMES	REMARKS
Pulse:				
Basal	182	65	45-105	0.6% above 100
Recumbent (medical examination) .	252	66	40-100	2.8% above 90
Sitting (medical examination) ..	252	73	48-105	6.3% above 90 and 2.4% above 100
Standing (medical examination) .	194	82	54-124	12.4% above 100
Sitting (before treadmill walk) .	127	84	50-124	14.7% above 100
Sitting* (before treadmill run) . .	231	90	55-136	26.4% above 100, including 6.1% above 110 and 3% above 120
Standing* (before treadmill run)	223	123	82-165	6.3% below 100
Systolic blood pressure:				
Recumbent	265	115	95-149	1.9% above 140 mm.
Sitting (medical examination)	253	123	100-155	4.7% above 140 mm.
Standing (medical examination)	194	121	90-174	7.7% above 140 mm.
Sitting (before treadmill test)	129	123	94-144	3.1% at 140 mm. and 0.8% above 140 mm.

*These measurements include college athletes.

and blood lactate after work. Taking into account these various factors, it was possible to determine how efficiently a man can perform exhausting work.³⁻⁶ Accordingly, the subjects were divided into four categories in regard to their performing capacity: poor, average, good and excellent.

Among the students the average basal pulse was 65, with a range from 45 to 105. The average sitting pulse at the time of the medical examination was 73, with a range from 48 to 105. Before the treadmill test, the average sitting pulse increased to 84 with a range from 50 to 124, and 19 subjects had a sitting pulse persistently above 100. In respect to their ability to do hard work, 3 of the latter were poor, 14 average, and 2 good. The performance capacity of the remaining 110 men whose sitting pulse was below 100 was distributed in about the same range. The average sitting pulse of the oarsmen before training was 84, with a range from 50 to 116. These values compare closely with the findings on the students. After training, the average sitting pulse of the oarsmen dropped to 67 with a range from 50 to 82. All these men were good or excellent in ability to perform on the treadmill. Although the average pulse is lower in oarsmen when under training, the pulses of certain students were often as high as in untrained students who were much less fit.

With a few exceptions, no satisfactory relation was found between basal pulse or sitting pulse and capacity to perform hard work (Figs. 1 and 2). Differences between sitting and lying pulses,

treadmill up to exhaustion or to a maximum of five minutes. This relation has been described,³⁻⁵ and the results of this study confirm the previous findings. Comparison of students with trained oarsmen shows that the average pulse of the stu-

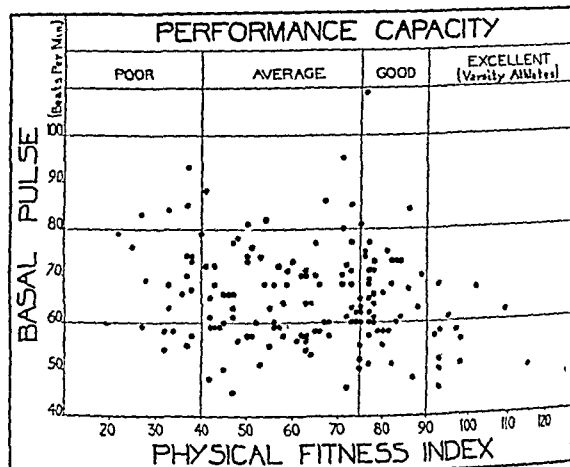


FIGURE 1. *Basal Pulse in Relation to Performance Capacity and Physical-Fitness Index.*

It should be noted that no significant relation exists between these measurements.

dents one minute after the run was 156, and of the oarsmen 130, whereas four minutes after the run the pulse was 114 for the students and 96 for the oarsmen. Individual pulses were regularly higher in the unfit subjects and lower in the fit (Fig. 3).

It is not commonly realized that in normal young men the maximum pulse during exhausting exercise may reach levels of 210 or more. In

the present series of 176 young men the maximum pulse (taken with the cardiographometer) during the run ranged from 167 to 217 with an average of 193 (Fig. 4). For a run of the same duration the maximum pulse of trained subjects is usually lower than that of untrained subjects.

The average sitting systolic blood pressure was 123 mm. for the students with a range from 102 to 144. The average blood pressure was the same for the oarsmen with a range from 112 to 136. No satisfactory relation could be found between these measurements and the performance capacity of the students or the oarsmen (Fig. 5). The diastolic

mill test: below 40, poor physical fitness; from 41 to 75, average; from 76 to 90, good; above 90, excellent.⁷

Figure 1 shows a lack of relation between the basal pulse and the physical-fitness index. Figure

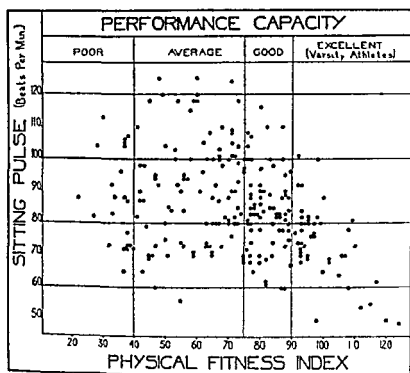


FIGURE 2 Sitting Pulse in Relation to Performance Capacity and Physical Fitness Index

It should be noted that, with the exception of 5 athletes who had pulses below 60 and at the same time a high index of fitness, no significant relation exists between these measurements

blood pressure also showed no relation to the physical fitness of these men. No definite relation was established between physical fitness and differences between systolic blood pressure standing and lying, a factor that is a part of the Schneider test.

On the basis of these results and similar experiments performed at the Harvard Fatigue Laboratory, an index of physical fitness for hard muscular work was computed by taking into account the duration of the run on the treadmill and the rate of the heart deceleration during the first period of recovery. This method has been described⁷ and has proved to yield valuable results in assessing that kind of fitness.^{8,9} The index is derived by dividing the duration of the run in seconds by the sum of three pulses counted at convenient intervals during the early recovery. The following interpretation is given to this index in the tread-

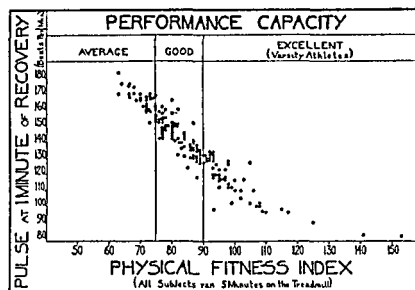


FIGURE 3 Pulse after Exercise in Relation to Performance Capacity and Physical Fitness Index

It should be noted that the men who were fittest had the lowest pulses in recovery.

2 shows a lack of relation between sitting pulse and the physical-fitness index, with the exception of 5 athletes who had a sitting pulse of 55 or below and a high fitness index. Pulses above 100 were found not only in the poor but also in the average and good groups, and even 2 varsity athletes had pulses of 100 and 102. Figure 3, on the contrary, shows a good relation between the pulse at one minute of recovery after the treadmill run and the performance capacity and the fitness

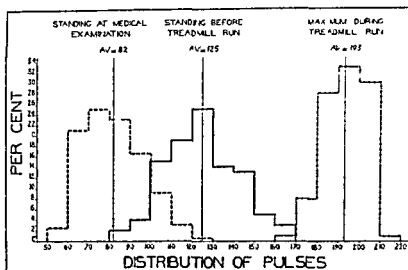


FIGURE 4. Distribution of Pulses of Normal Young Men under Various Conditions.

index. Figure 5 shows no satisfactory relation between the sitting systolic blood pressure and the fitness index. Systolic blood pressures equal to or above 140 mm. are found in subjects who rank poor, average or good in fitness, and systolic blood pressures of 110 mm. or less are also found in the various groups.

Therefore, there is obviously no satisfactory relation between physical fitness for hard work and basal or sitting pulse rates or sitting blood pressures. In contrast, the pulse during recovery from hard exercise shows a good relation to a man's fitness for strenuous exertion.

INFLUENCE OF EMOTIONAL FACTORS ON RESTING PULSE AND BLOOD PRESSURE

Although the influence of common emotional factors on the heart rate at rest is well known,^{4, 10, 11} it is too often underestimated. The two following

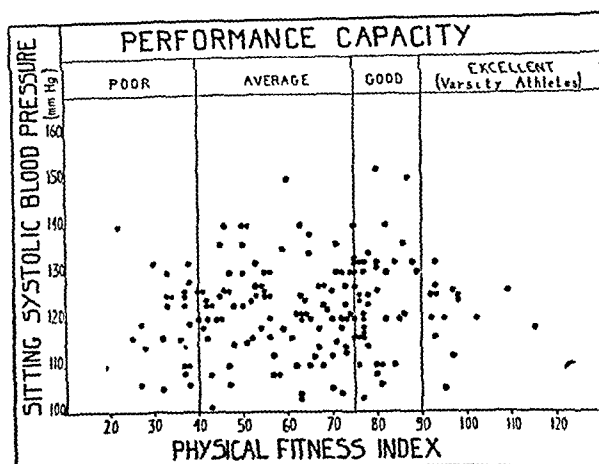


FIGURE 5. Sitting Systolic Blood Pressure in Relation to Performance Capacity and Physical-Fitness Index.

It should be noted no significant relation exists between these measurements.

sets of results emphasize the importance of these factors in determining the heart rate of subjects who are not actually working.

The sitting pulse was recorded on 231 subjects resting for ten minutes before the treadmill run but after a warming up, which consisted in walking at 3 miles per hour, grade 8.6 per cent, on the treadmill. In 61 of them the lowest pulse was above 100 beats per minute. Fourteen of the latter men were poorly fit, 36 were average, 10 were good, and 1 was excellent. In comparison, the men who had pulse rates well below 100 under the same conditions had a similar performance capacity. Since no physical work accompanied the rise of pulse, it is seen that the emotional effect of being tested was the factor responsible for the increase of heart rate. The conclusion that this is an emotional effect* is further illustrated by the fact that 20 per cent of subjects had a lower heart rate during

the rest period after walking on the treadmill than before walking, and that about 10 per cent of them had a lower sitting pulse five to seven minutes after an exhausting run than before the run. Such findings clearly indicate that in these subjects the high heart rates before the test were due to persistent emotional stimulation.

Heart rates were also recorded by the cardio-tachometer before the beginning of the treadmill run, with the subject standing on the treadmill ready to go but motionless. The pulse per minute was derived from twelve-second recordings. Under these conditions the average pulse in 170 students was 125, with a range from 82 to 165 (Fig. 4). Only 8 subjects had a pulse below 100. Four minutes after the treadmill run the average pulse was only 113 with a range from 78 to 150.

The same phenomenon can be observed both in nonathletic students and in well-trained athletes. For example, in the oarsmen the average pulse standing on the treadmill was 120 (extremes 108 to 135), and four minutes after the run it was reduced to 96 (extremes 63 to 108). In 30 cross-country runners, the average pulse standing on the treadmill was 114 (extremes 96 to 140), and four minutes after the run it was 101 (extremes 80 to 120) (Table 1).

These observations show that in young men emotional factors markedly influence the heart rate at rest before a test of physical fitness. Such factors are probably largely responsible in determining the heart rate during the course of a routine medical examination.

Similar observations have been made by Dr. J. R. Gallagher,¹² of Phillips Academy, Andover, Massachusetts, on boys ranging from twelve to eighteen years of age. The resting pulse taken at the time of the annual medical examination varied from 48 to 125. Eighteen boys out of 726 had pulse rates persistently over 100. In 14 of them the pulse was between 100 and 109, 2 had pulse rates between 110 and 119, and 2 had resting pulse rates between 120 and 125. Furthermore, 11 boys had resting systolic blood pressures of 140 mm. or more. The increase of pulse before the test of physical fitness was regularly observed. All of them nevertheless were medically normal and well within the usual range of physical fitness for that age group, as measured by their actual capacity to perform a standard amount of hard work.

SUMMARY AND CONCLUSIONS

There is a wide variation in pulse and blood pressure in normal, healthy young men. Although the values far exceed the usually accepted norms, they are nevertheless compatible with nor-

* "Emotional effect," as employed here, in no way conveys the idea of a psychiatric abnormality. It refers to the apprehension, excitement and the variation that may be carried by it. A detailed psychiatric purpose, revealed no

mal physiologic reactions to emotional stress and hard muscular work.

There is no satisfactory relation between basal pulse, sitting pulse and physical fitness for strenuous exertion in normal, healthy young men.

There is no relation between sitting systolic or diastolic blood pressure and physical fitness for strenuous exertion in normal, healthy young men.

Emotional factors are largely responsible for high resting pulse rates commonly found during the preinduction medical examination of healthy young men.

Resting pulses above 100 and sitting systolic blood pressures above 140 mm. are not exceptional in medically normal subjects when exposed to some emotional strain and in many of them they accompany an average or good physical fitness for hard muscular work.

In normal young men no measurement of pulse or blood pressure, taken at rest, is indicative of capacity to perform hard work.

When the resting pulse or blood pressure is unusually high it is recommended that the subject

be submitted to a standard amount of strenuous exercise. The estimate of capacity to do hard muscular work should be based on the subject's actual ability to perform it and on the speed of recovery of his heart after exercise, rather than on resting values of pulse and blood pressure alone.

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DIABETES MELLITUS IN GENERAL PRACTICE*

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IN THE time allotted for this discussion I shall not dwell upon the history of diabetes mellitus, the older conceptions of the disease, or its displaced methods of diagnosis and treatment. It suffices to say that the knowledge of diabetes has come a long way from the time when it was the custom of physicians to decide that sugar was present in the urine from its syrupy appearance and sweet taste. It is doubtful if there is anyone present who has ever had the temerity to maintain that such a diagnosis could be made on that evidence alone. Yet the doctors of other days were not inhibited by refined sensibilities which we apparently possess to a greater degree, and no doubt we have sacrificed something of value in the process of evolution. I am assuming that every modern practitioner is aware of the method of diagnosis of diabetes long before the patient has reached the stage where there is inordinate thirst, excessive polyuria and marked loss of weight; and that all are aware of the value of routine urine examinations, of the taking of night and morning specimens in suspicious cases rather than a single

specimen at any one time of day, and of blood chemistry both in diagnosis and during treatment. Within the experience of most of us has occurred the discovery of insulin and the revolutionizing of the treatment of diabetes, so that now it is rare for a patient to die from the effects of diabetes alone. To younger practitioners this is simply a matter of historical interest, since during their training and recent years of practice they have known no other way of approaching diabetes.

That so large a number of diabetic patients who previously would have died in the course of a few years now come within the age groups susceptible to cancer, arteriosclerosis, heart disease and other degenerative ailments affecting the vital statistics of these groups, is mentioned only in passing. Assuming, therefore, a general acquaintance with the essential knowledge of diabetes at present,—that is, its symptoms, its effects and the tests required to confirm its presence, I approach the subject with the flat assertion that any general practitioner who will give the time and thought to diabetes that it requires is qualified to treat the disease on relatively equal terms with the specialist. The average case that goes along smoothly with the diabetic expert

*Read at a meeting of the Worcester District Medical Society, Worcester, Massachusetts, April 15, 1942.

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should go just as smoothly with the general practitioner, and any case that baffles the latter likewise, and to the same extent, baffles the former.

In the majority of cases of diabetes, it is not essential to begin treatment with a period of hospitalization, although in many cases this is desirable. Only 9 patients of the series reported below have ever been hospitalized for any condition connected with diabetes. This policy will appear debatable to many, but these cases are presented exactly as they occurred.

Of the 63 cases covered by this paper, — 5 patients under five years of age are included, — only one is reported in each of several groups, formed according to type and severity. Except for minor variations, these cases are representative of the various groups.

CASE 1. M. R. Y., a 47-year-old, unmarried woman, was first seen on August 15, 1938. She had lost 25 pounds in the previous 4 months. She tired easily during the previous 2 months, but had no headache or sleepiness, and had moderate thirst. She was nervous and irritable, slept badly, and had a poor appetite, and her bowels were normal. There was occasional nocturia. Five years previously she fell from a horse, receiving a possible fracture of the skull. She returned to her work as a nurse 1 month later, but had not been well since. The sense of smell was absent for 2 years and was still abnormal.

Physical examination showed a thin, poorly nourished woman 5 feet 5 inches in height and weighing 98 pounds. The pulse was 104 and the blood pressure 156/74. The urine showed a specific gravity of 1.040, was acid and contained no albumin and 5 per cent sugar. The fasting blood sugar was 212 mg. per 100 cc.

The patient was placed on a 1775-calorie diet and given insulin, 15 units three times a day. Four days later the blood sugar was 104 mg. per 100 cc. and the urine was negative for sugar. She was intelligent and co-operative, and understood perfectly the value of the diet for maintaining normal weight, and the necessity of daily watchfulness with regard to the urine. With the advent of protamine-zinc insulin the patient began taking it in daily doses of 30 units each, supplemented by 8 to 15 units of regular insulin when sugar showed in the urine at the noon or evening meal.

Subsequent blood-sugar readings ranged from 105 to 182 mg. These were first taken at monthly intervals, but are now taken only when there is a stubborn increase in the urinary sugar output. The weight has been maintained at 123 pounds, from which there is practically no variation. A high level of blood sugar has occurred only during the course of upper-respiratory irritation, or following trips away from home, during which the diet may be variable.

CASE 2. F. B., a 64-year-old, married woman, was first seen on May 6, 1940, complaining of headache, exhaustion and pain in the legs. She had known for 11 years that her urine contained sugar, and during the last 2 years had been a patient in the Webber Hospital, Biddeford, Maine, and in the Deaconess Hospital, Boston. Control of her disease had apparently been difficult in both places, and she had been subject to almost daily insulin-shock reactions.

Physical examination showed a poorly nourished woman 5 feet 4 inches tall and weighing 94 pounds. The pulse was 88 and the blood pressure 194/110. There was marked arteriosclerosis.

It was decided that the patient would maintain her weight at 110 pounds on a 1775-calorie diet. The blood sugar at the beginning of treatment was 188 mg. per 100 cc. and the sugar in the urine 3 per cent. She was placed on a morning dose of 30 units of protamine-zinc insulin and 15 units of regular insulin. Although she insisted she could not eat the amount of food on her diet list, she was compelled to eat it. The weight rapidly rose to 109 pounds, and has been maintained at that point to the present time. One and a half grains of Digitoxin was given daily for irregularity of the heart, but nothing was done for the arteriosclerosis or hypertension. The urine was tested at noon and night, and an additional 15 to 18 units of regular insulin was given when sugar was present. Blood-sugar tests taken at intervals of two to four weeks showed variations from 100 to 232 mg. per 100 cc., the last high reading being on September 27, 1941.

The patient has had only two insulin reactions of a minor type, which followed the discovery of a blood sugar of 212 mg. in September, 1941, when the protamine-zinc insulin dose was increased to 40 units and the blood sugar dropped rapidly to 108 mg. Orange juice was effective in quickly combating these insulin shocks, and the blood sugar on October 18 being 100, the 30-unit dose was resumed. The patient at present shows a small trace of albumin in the urine, traces of sugar several times a week and a blood sugar of 130 mg. She is in excellent condition.

CASE 3. M. H., a 67-year-old, married woman, was first seen on January 15, 1934, with a history of intermittent glycosuria since 1926. She complained of severe abdominal and epigastric pain, backache, headache and dizziness, with some sleepiness and weakness. Analgesics gave no relief for the pain, and urine examination showed large amounts of sugar. The blood-sugar content was 325 mg. per 100 cc.

On diet and insulin the body weight was reduced from 178 to 149 pounds, but as soon as the patient felt better, she refused to follow the prescribed diet or to take insulin in proper doses. At intervals of 4 to 6 months she had recurrences of abdominal pain. As a result she became more co-operative until once more free from symptoms, when she again broke all the rules. In 1941 she was hospitalized for gangrene of a toe, which was amputated. She is now sugar-free, but will undoubtedly break the rules again and have further trouble with her extremities.

CASE 4. O. T., a 40-year-old, married woman, was first seen in 1922, when, at the age of 18, she had an acute attack of weakness, thirst, weight loss and large amounts of sugar in the urine. As often occurs in younger people developing diabetes, she requires at present in order to maintain her proper working weight relatively large doses of insulin, namely, 35 units of protamine-zinc insulin and 20 units of regular insulin before breakfast and 15 to 25 units of regular insulin before supper, according to the color test of the urine. However, she is able to do clerical work during the day, and in addition does her home cooking and housework. The blood sugar has ranged from 238 mg. to a maintenance level of 106 mg. per 100 cc.

CASE 5. F. E. P., a 54-year-old man, first seen in 1932, developed symptoms of frequency of urination and pruritus on the inside of the thighs, with nocturia and a feeling of fatigue and thirst. The urine sugar was 5 per cent

and the blood sugar 294 mg. per 100 cc. With insulin and diet the blood-sugar level in 19 days was reduced to 150 mg., and for the following 3 months remained at about that level. Meanwhile the urine was sugar free. At a blood-sugar level of 111 mg., with sugar-free urine, insulin was discontinued and the urine remained sugar free for more than a year without the ingestion of more insulin. Since then, it has been necessary to give insulin for only 6 weeks out of each year.

Comment. This case exemplifies the oft-repeated observation that there is no definite relation between blood-sugar findings and urinary sugar: with a high urine sugar the blood sugar is often comparatively low, and *vice versa*.

DISCUSSION

Among the 63 cases of diabetes treated in this series, there were 5 deaths (8 per cent). The average age at diagnosis was fifty-one years, and the average known duration of the disease was seven years. The latter figure is not a reliable index of actual duration, because no doubt many of the milder cases had existed for some time before discovery. The average age at present is fifty-eight, the youngest patient being twenty-four and the oldest seventy-eight. There were 7 men and 56 women. In 2 cases both husband and wife had diabetes. The average body weight at onset was 169 pounds, with the highest 235 and the lowest 90 pounds. The average weight at present is 150 pounds with the highest 190 and the lowest 110 pounds. The average daily intake of insulin is 22 units, with the highest 65 units. No insulin is now being taken in 6 cases, and less than 15 units in 2. The average blood sugar on diagnosis was 196 mg. per cent—the highest 325 mg. and the lowest 120 mg. The average maintained level of blood sugar in all cases was 120 mg., with the lowest 100 mg. and the highest 137 mg.

The causes of death were as follows: carcinoma of the liver and pancreas (age fifty-seven); general carcinomatosis with cerebral hemorrhage and paralysis (age sixty-nine); general carcinoma, myocardial failure with ascites (age sixty-eight); lobar pneumonia (age sixty-four); and coronary thrombosis (age sixty-seven).

Other diseases or conditions associated with diabetes at the time of diagnosis were: arteriosclerosis, 8 cases; cholelithiasis, 1 case (operated on and cured); cholecystitis, 1 case (not operated on); hypertensive heart disease, with or without valve lesions, 4 cases; varicose veins, 5 cases; varicose ulcers, 1 case; arthritis, 5 cases; carcinoma, 3 cases (all the patients died of carcinoma within

an eight-year period); hemorrhoids, 1 case; gangrene of great toe, 3 cases (one of these patients was operated on and the toe removed; another was removed to Florida and arrangements were made for her hospitalization; the third patient, whose diabetes was discovered at the time the gangrenous toe was observed, has, under the intensive use of insulin and care, preserved the toe, although it is expected that the slightest bruise or disturbance of the circulation will lead to its loss); myalgia, 1 case; pilonidal cyst, 1 case (operated on and cured); carbuncle of the neck, 1 case severe but cured); carbuncle of the shoulder, 1 case (very large, and in sloughing out left a large cavity, which was slow to heal).

With the control of diabetes there has been a marked decrease in diabetic mortality and an increase in the complicating diseases associated with it, particularly the carcinomas and degenerative diseases incident to the prolongation of life in these patients.

It may be said that diabetic patients who are treated well may carry on effectively and do work that is not noticeably less efficient than that of their diabetic-free neighbors. In fact, work is in itself excellent medicine. The nonintelligent diabetic patient presents a problem that can be solved only by having an intelligent member of the family watch the diet and supervise the testing of urine and the giving of insulin.

The classic definition of diabetes mellitus is "a metabolic disorder in which the ability to oxidize carbohydrates is more or less completely lost due to faulty pancreatic activity, especially of the islets of Langerhans." This produces hyperglycemia with resulting glycosuria and polyuria giving symptoms of thirst, hunger, emaciation and weakness and also imperfect combustion of fats with resulting acidosis, resulting in the symptoms of dyspnea, lipemia, ketonuria and finally coma. There may also be pruritus and lowered resistance to pyogenic infections. But the alert practitioner will diagnose many cases of diabetes mellitus long before these later symptoms appear. In fact, most cases should be diagnosed before the patient is markedly ill, or aware that he is sick. Routine urine examinations on all cases, either at home or in the doctor's office, should be done not later than the second call. In this way an unbelievable number of unsuspected cases of diabetes can be discovered.

125 Main Street

CLINICAL NOTE

ADDISON'S DISEASE: REPORT OF A FATAL CASE*

L'EUTENANT COLONEL HERMAN A. LAWSON,
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THE following case report of fatal Addison's disease is presented because of the relative rarity of some of the findings, and because its occurrence in a soldier on active duty seems worthy of note.

CASE REPORT

C. P. N., a 29-year-old private in a military police company, was admitted to the Medical Service of the 48th Evacuation Hospital on September 11, 1942, for symptoms of shock of 12 hours' duration. The hospital was located near Murfreesboro, Tennessee, and was acting as an evacuation hospital for the training maneuvers of the Second Army.

The patient had been well until 4 days before admission, when he complained of nausea and vomiting. He was taken to a medical field station the night before admission, and a history of low-abdominal pain and constipation for a few days preceding was elicited. An enema was administered, and immediately after this the patient went into a state of shock. He was given shock treatment and appeared to improve considerably, but relapsed on the following morning and was evacuated to the hospital.

Subsequent to the death and autopsy, additional information was obtained from the patient's commanding officer to the effect that about 4 weeks before the terminal illness he complained of weakness, extreme fatigability, abdominal pain, diarrhea and nervous irritability, and became exceptionally pale. He was sent to sick call on August 14 and again on September 3, at which time marked fatigability and weakness were noted. On the latter day he went on a short hike with his company, but had to be returned to the company area because of weakness.

On physical examination at admission the patient appeared extremely weak, but was able to talk rationally. The temperature was 97.5°F., the pulse 140 and feeble. The systolic blood pressure was 80. The head showed no signs of external violence. The pupils reacted to light and were of normal size. Both eyeballs were soft and sunken into the orbits. The ears, nose and throat were normal. No mucosal pigmentation was noted. The breath had an acetone odor. The skin was pale, cool and dusky. The mucous membranes and nailbeds were cyanotic. No abnormal cutaneous pigmentation was noted. The neck showed no stiffness or enlarged nodes. The heart was normal in size. The sounds were faint and no murmurs were heard. The lungs were resonant. Breath sounds were heard with difficulty because of shallow respirations. There were no rales. The abdomen was

negative. The extremities showed no edema. The tendon reflexes were absent. There were no abnormal reflexes.

The white-cell count was 14,700, with 56 per cent (2 per cent segmented and 54 per cent stab forms) neutrophilic leukocytes, 40 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils.

The admission diagnosis was shock and dehydration of undetermined origin. Among the possible causes suggested were overwhelming sepsis, poisoning, rupture of the colon or other viscus and acute adrenal insufficiency.

The patient received 2000 cc. of 5 per cent glucose in normal saline solution intravenously, two ampules of caffeine sodium benzoate intramuscularly, warmth, and elevation of the lower extremities. Nasal oxygen was administered, which relieved the cyanosis. Soon after admission the pulse became imperceptible and the blood pressure unobtainable. Over the course of the next few hours the patient's condition grew rapidly worse. No urine could be obtained, even with an indwelling catheter. The respirations became rapid, and moist rales were audible in the lungs. The skin remained cool. The patient's mental state became clouded, coma supervened, and he died 6 hours after admission. A blood culture taken post mortem was negative; the nonprotein nitrogen was 36 mg., the blood sugar 109 mg., and the urea nitrogen 11 mg. per 100 cc.†

Autopsy (performed 3 hours after death). The following is a summary of the gross findings, which were as follows:

The body appeared well developed and well nourished, but the infrahollows appeared increased. The hair was prematurely gray. The subcutaneous fat appeared to be of normal thickness. Abnormal pigmentation of the skin and mucous membranes was not found. The parietal and visceral pleura were adherent owing to diffuse fibrous adhesions on all surfaces, which were separated by blunt dissection with great difficulty. The interlobar pleural surfaces showed similar adhesions.

The right lung weighed 704 gm. and the left lung 640 gm. Both lungs showed markedly thickened pleura, especially over the upper lobes. A few pea-sized, blackish perihilar nodes were noted that showed no caseation or calcification on section. All the bronchi were filled with bloody froth. The parenchyma was hyperemic, especially in the lower lobes. There was no evidence of chronic parenchymatous disease.

The heart weighed 320 gm. and showed no abnormalities. The aorta was normal. The periaortic nodes of the thoracic aorta were increased in size and number. No caseation was seen on section. The spleen weighed 210 gm. and showed no abnormalities. The liver weighed 1664 gm. There were no abnormalities in the liver, pancreas, gastrointestinal tract or kidneys, each of which weighed 160 gm. The lymph nodes of the mesenteric root appeared slightly increased in size and number. They showed no caseation on section.

The adrenal glands both showed identical findings and were surrounded by indurated fat. The capsules were markedly thickened. The parenchyma was almost entirely replaced by grayish, cheesy, crumbly material, which showed a tendency to shell out. No remaining medulla was discernible, but in one area in the right gland there was a small island of apparently normal cortex. Crushings of the cheeselike material from each gland were negative for acid-fast bacilli.

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†These examinations were performed by H. T. Hart, United States Veterans' Hospital, Murfreesboro, Tennessee.

Gross diagnoses: Bilateral caseous tuberculosis of adrenal glands; acute pulmonary hyperemia; bilateral chronic fibrous pleuritis.

Microscopic examination was performed by the laboratory of the Lawson General Hospital, Atlanta, Georgia. It was reported as follows:

The adrenal glands are almost entirely destroyed. They have been replaced with a necrotic granulomatous tissue appearing fairly characteristic of tuberculosis. Ziehl-Neelsen stain revealed a rare tubercle bacillus. A hilus lymph node and one other node show a chronic tuberculosis. Other nodes are not involved. The sections of lungs show acute congestion with no evidence of tuberculosis. The sections of the heart, liver, kidney and spleen appear essentially normal.

Anatomical diagnoses: Tuberculosis of adrenal glands (Addison's disease); tuberculous lymphadenitis.

The Army Medical Museum in a communication to the Lawson General Hospital reviewed this case as follows:

Diagnosis: Addison's disease secondary to bilateral involvement of the adrenal glands. The latter present characteristic areas of caseation necrosis with typical tubercle formation. The greater portion of the cortex is completely destroyed in this process, although occasionally small hyperplastic accumulations of cortical cells still persist. In the lymph nodes one recognizes not only tuberculous foci but in addition small areas of amyloid deposition. It is interesting to note the absence of any recent tuberculous lesion in the lung.

DISCUSSION

The absence of visible abnormal pigmentation in this patient is contrary to the usual expectation. Although Lewin (quoted by Grollman¹) found pigmentation in only 72 per cent of his autopsied cases, this figure is generally held to be far too low. Thus Rowntree and Snell² in their series of 108 cases had only 1 case without pigmentation, and Means³ states that only rarely are cases of the chronic form found without pigmentation. Pigmentation is generally one of the first symptoms to appear and may, in fact, antedate other symptoms by months or even years. In this case, although symptomatically of short duration, the destructive process in the adrenal glands was undoubtedly chronic, and should have afforded ample time for the formation of the abnormal pigmentation. The cause of the pathologic pigmentation in Addison's disease has never been satisfactorily explained,⁴ and hence no theory can be advanced for its nonappearance in this case.

Another aspect of this case worthy of note is the relatively short duration of the clinical symp-

toms. The case of shortest duration on record is eighteen days.⁵ Our patient made his first appearance at sick call four weeks before admission, and was not sick enough to warrant hospitalization until the night before his death. This is especially significant, because it is usual Army procedure, especially when troops are on maneuvers, to evacuate and hospitalize personnel not capable of full duty. There was no known precipitating factor such as infection, exposure or medication to account for the sudden fatal Addisonian crisis. It seems unlikely that such trivial bodily trauma as that caused by an enema could have been the precipitating factor.

It is remarkable that the patient continued active as long as he did, in view of the practically complete destruction of adrenal tissue. As no adrenal rests were detected at autopsy, it can be inferred that the minute hyperplastic remnants of cortex produced sufficient hormone to maintain life and a fair degree of activity.

No facilities for the analysis of the blood sodium or chloride were available, but it is noteworthy that the results of the blood chemical tests that were made were contrary to the usual findings in Addisonian crisis. There was no abnormal nitrogen retention or hypoglycemia.

A similar case is cited by Boyd.⁴ This patient was also a soldier and was carrying on his duties in a camp. He was found in a semiconscious state and died in a few hours. The adrenal glands were found to have been completely destroyed by tuberculosis, and there was no trace of pigmentation.

SUMMARY

A case of rapidly fatal Addisonian crisis due to tuberculosis of the adrenal glands in a soldier on active duty is reported as noteworthy, because of the complete absence of pathologic pigmentation, normal blood sugar and blood urea nitrogen and an ascertainable clinical history of only four weeks.

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MEDICAL PROGRESS

ISOTOPES IN MEDICAL INVESTIGATION AND THERAPY (Concluded)*

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EYE

THE prevention and treatment of glaucoma and of many other ophthalmologic diseases can be placed on a sound physiologic basis only when there is a complete understanding of the mechanisms of water and ionic exchange between the fluids of the eye and the blood stream. Important contributions to the current knowledge of such exchange have been made by Kinsey, Grant and Cogan.²³ These investigators injected heavy water intravenously into rabbits and followed its appearance in the aqueous and vitreous of the eye. In another series of experiments, they replaced some of the fluid of the aqueous and vitreous with isotonic sodium chloride containing heavy water and traced the disappearance of the labeled material from the eye. Exchange of water between the aqueous and the blood was extremely rapid, half of the water content of this fluid being replaced in less than three minutes, a rate of exchange fifty times greater than that previously reported for the rate of formation for the whole aqueous.

The quantity of water going from the aqueous to the vitreous and to the lens was found to represent only a small portion of the total water movement out of the aqueous. The rate of exchange of water by the vitreous was considerably slower, ten to fifteen minutes being required for a 50 per cent replacement.

Net transfer of water through the cornea has been believed to occur only from the posterior to the anterior surface, the direction of transfer apparently being determined by the integrity of the corneal epithelium, which maintains osmotic pressure by its semipermeability. Previous attempts to demonstrate passage of water in the anteroposterior direction have been unsuccessful because bullae and epithelial damage resulted as soon as the concentration of sodium chloride became greater on

the posterior surface of the cornea than it was on the anterior surface. Using heavy water, it has been shown that water passes through the cornea in both directions, but that the normal epithelium is essentially impermeable to passage of sodium chloride in either direction.²⁴

Radioactive sodium, chloride and phosphorus passed into the anterior chamber much more slowly than did water.²⁵ The sodium and chloride ions entered the anterior chamber at a rate calculated to be equivalent to 4 cu. mm. per minute of whole aqueous, a rate that is of the same order of magnitude as the rate of formation of the whole aqueous. These findings indicate that "the apparent rates of aqueous formation are more directly concerned with electrolyte net volume changes than with water movement, which is only coincidental."

TEETH

Interest in the pathologic physiology of dental caries has stimulated considerable investigation of the mineral metabolism of the teeth. To date much of this work has been concerned with determining the mode of deposition of phosphate in the enamel and dentin. Early in vitro studies showed that both the dentin and enamel adsorbed phosphates from aqueous solutions, the phosphate ions being deposited on a crystal latticework of hydroxyapatite in such fashion that the calcium-phosphate ratio was maintained at 2.10 in both tissues, although deposition occurred more rapidly and in larger amounts in the dentin than it did in the enamel.²⁶ These findings suggested that adsorption of various minerals from the saliva might occur, and animal experimentation demonstrated this fact. Sognnaes and Volker²⁷ found that radioactive phosphorus appearing in the surface layers of enamel in various animals was definitely adsorbed from the saliva. Larger amounts of phosphate were deposited in the dentin, and it was believed that it reached this tissue from the blood stream. More recent studies by Barnum and Armstrong²⁸ showed that although some of the phosphate of the enamel was adsorbed from the

*The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942, \$5.00).

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saliva, the major portion was derived from the blood and passed through the dentin before reaching the enamel. They also found, however, that phosphate could pass from the saliva through the enamel and into the dentin. These findings held for mature nongrowing teeth as well as for the actively growing teeth of young animals, proving that even the highly mineralized dental enamel is not static but is in a state of constant mineral exchange and replacement.

Fluorides are in some way related to the inhibition of dental caries. The addition of a fluoride to caries-producing diets greatly decreases the incidence of dental caries. Persons living in districts in which water and diet contain large quantities of fluorides develop dental caries much less frequently than do the inhabitants of areas in which fluoride concentration is normal or low; and finally, chemical analyses show that the enamel of sound teeth contains more fluoride than does carious enamel. These facts suggest that dental caries might be prevented or controlled if fluoride could be deposited therapeutically in the enamel. Volker and his associates²⁹ showed that significant amounts of fluoride were deposited in the enamel after parenteral administration or after local application of fluoride solutions directly to the teeth. The possible widespread prophylactic or therapeutic use of fluorides has at least one serious drawback, however, since deposition of even small amounts of fluoride in the teeth produces an extremely unsightly, although harmless, condition known as "mottled enamel" or "dental fluorosis."

CIRCULATION OF BLOOD AND SPLENIC FUNCTION

The blood volumes of animals and of human subjects have been determined by injecting erythrocytes labeled with radioactive iron^{30, 31} or radioactive phosphorus³² into experimental subjects and determining dilution of radioactivity produced by the blood of the recipient. Such experiments indicated that the actual volume of erythrocytes present in the circulatory system was only three quarters of the volume calculated by the dye-dilution technic. This entire volume of cells appeared to be in active circulation, and there was no evidence that cells were stored in the spleen or in any other hypothesized reservoir.³⁰

A constant relation between the volume of cells in the circulation and the venous hematocrit has been demonstrated by Hahn and Bale.³³ These investigators³¹ also showed that the total blood volume of the dog was constant, in spite of the marked variations in the relative proportions of cells and plasma that occurred during periods of anemia.

The astonishing fact that in the guinea pig a volume of water equal to 66 per cent of the total blood volume was exchanged with the extravascular fluid every minute was demonstrated by Flexner, Gellhorn and Merrell.³⁵ The great rapidity of this exchange was discovered by injecting heavy water intravenously and determining the length of time required for establishment of equilibrium between the blood and the extravascular fluid. Similar technics could readily be applied to human subjects using not only heavy water but labeled electrolytes and other substances. Such experiments would be of interest in studying conditions in which there is a supposed disturbance of vascular permeability.

An objective method for determining the circulation time in infants and children has been developed by Hubbard, Preston and Ross.³⁶ Radioactive sodium was injected intravenously into the antecubital vein of one arm, and the length of time required for radioactivity to appear in the blood of the other arm was measured. Although this method appears feasible, technical complexities limit its extensive use, and it is probable that the much more easily performed fluorescein method is just as reliable.

It has been assumed that the spleen serves as a reservoir for the storage of a large volume of erythrocytes, and that by muscular contraction it can express these stored cells into the circulation during times of stress. The finding that all the erythrocytes in the vascular system appear to be in active circulation³⁰ casts doubt on this theory. Experiments with radioactively tagged erythrocytes demonstrated that adrenalin injection and exercise did not produce any increase in the total volume of circulating erythrocytes, even though these procedures caused transient increases in the hematocrit.^{37, 38} Ross and Chapin³⁰ found that the increase in the hematocrit produced by injecting adrenalin intravenously into human subjects was associated with a simultaneous and identical increase in the concentration of the plasma proteins, and that these changes were not influenced by splenectomy. They suggested that this hematocrit change is the result of hemoconcentration and not of splenic contraction, and concluded that the spleen does not function as a reservoir for the storage of any significant volume of erythrocytes.

ERYTHROCYTES

The rapidity with which hemoglobin can be formed was indicated by the appearance of radioactive iron in the hemoglobin of circulating erythrocytes four hours after the isotope had been ingested.^{40, 41} Since the iron of the hemoglobin molecule does not exchange with plasma or tissue

iron,⁴² this observation showed either that the mature red blood cell synthesized hemoglobin, or that the rate of maturation of the cell was extremely rapid. The administration of large quantities of iron therapeutically accelerated the rate at which labeled iron was incorporated in erythrocytes, suggesting a stimulating effect of iron on hematopoiesis.⁴⁰

The iron liberated by the breakdown of erythrocytes is rapidly reutilized by newly formed erythrocytes in preference to iron present in the usual tissue stores.⁴³ Although the exact interpretation of this finding is not clear, it may indicate that the hematopoietic system is able to reutilize some of the iron-containing products of hemoglobin breakdown before they have been completely degraded.

INTERMEDIARY METABOLISM

The entire concept of the intermediary metabolism of carbohydrate, protein and fat and of the intricate biochemical processes by which life itself is maintained must be completely revised. The theory of independent exogenous and endogenous types of metabolism, the first concerned with wear and tear and replacement of the structures of the body, and the second with the supply of energy by combustion of foodstuffs, must be abandoned. In its place one must substitute the concept of a dynamic body equilibrium, a delicately balanced and infinitely complex chemical system in which all reactions are interdependent, but so adjusted that the body components remain constant in total amount and structure.

This fundamental and revolutionary revision of the concepts of metabolism has been brought about chiefly by the epoch-making experiments of Schoenheimer and his associates, employing heavy isotopes as labeling agents. In a series of well-integrated experiments, these investigators demonstrated that all body constituents are in a state of constant flux and change. Schoenheimer⁴⁴ has concisely summarized these contributions in the following paragraph:

The large and complex molecules and their component units, fatty acids, aminoacids and nucleic acids, are constantly involved in rapid chemical reactions. Ester, peptide and other linkages open; the fragments thereby liberated merge with those derived from other large molecules, and with those absorbed from the intestinal tract, to form a metabolic pool of components indistinguishable as to origin. These liberated molecules are again subject to numerous processes. Fatty acids are dehydrogenated, degraded or elongated, and thereby continually interconverted. While some individual molecules of these acids are completely degraded, other individuals of the same chemical species are steadily formed from entirely different substances,

notably from carbohydrate. Similar reactions occur among the split products of the proteins. The free aminoacids are deaminated, and the nitrogen liberated is transferred to other previously deaminated molecules to form new aminoacids. Part of the pool of newly formed small molecules constantly re-enters vacant places in the large molecules to restore the fats, the proteins and the nucleoproteins. Some of the small molecules involved in these regeneration reactions constitute intermediate steps in the formation of excretory products.

The intermediary metabolic reactions of sulfur-containing compounds⁴⁵ and of phospholipids⁴⁶ also conformed to the concept of metabolic regeneration.

The ability of the animal organism to utilize the completely oxidized carbon atom of carbon dioxide for the synthesis of glycogen has been demonstrated by Hastings and his associates.^{47, 48} They injected a solution of sodium bicarbonate labeled with radioactive carbon into rats and subsequently detected the labeled carbon atoms in glycogen isolated from the liver, a truly revolutionary discovery, since all previous concepts of carbohydrate metabolism had regarded the completely oxidized carbon of carbon dioxide as a waste product.

In subsequent experiments⁴⁹⁻⁵¹ it was discovered that carbon dioxide entered into the formation of glycogen by a process of condensation with pyruvic acid to provide the 4-carbon acids essential for glycogen synthesis. Other investigators⁵² found that isolated slices of liver tissue retained the ability to convert carbon dioxide into carboxyl and carbonyl carbon. The architectural structure of the liver was not essential for this conversion, since it occurred in both minced liver tissue and cell-free liver extracts.⁵³

The importance of these experiments can scarcely be overestimated, since they necessitate complete revision of our present concepts of carbohydrate metabolism.

THERAPEUTIC APPLICATIONS

Radioactive isotopes are effective therapeutic agents only if they are selectively deposited in the neoplastic or hyperplastic tissue that is to be destroyed. They must be deposited in such tissue in a much higher concentration than in normal tissue if radiation is to destroy the diseased tissue but not the normal tissue. Finally, the radiations that such isotopes emit must be strong enough to inhibit the growth of or actually to destroy the cells. To date only three isotopes, radioactive phosphorus, radioactive iodine and radioactive strontium, have fulfilled these requirements.

Radioactive phosphorus is deposited in high concentration in the rapidly growing cells of leu-

kemic and lymphomatous tumors as well as in the bone marrow and bone of leukemic and polycythemic patients.^{64, 65} In these sites it liberates fairly destructive radiations that inhibit or destroy the actively growing tumor and bone-marrow cells. Radioactive phosphorus has been used extensively in the treatment of malignant diseases of the leukemia-lymphoma type by several groups of investigators,⁶⁶⁻⁶⁹ who have recently summarized their experiences with 300 patients so treated. Their reports are fairly uniform concerning the effectiveness of the therapy in various diseases. Radioactive phosphorus is undoubtedly of considerable value in the treatment of lymphosarcoma and the chronic forms of myelogenous and lymphatic leukemia. It has on a few occasions produced remarkable remissions in acute leukemia but, on the whole, has been no more satisfactory than x-ray treatment in the control of the disease. Primary and metastatic carcinoma, Hodgkin's disease, multiple myeloma, reticulum-cell sarcoma and malignant melanoma have failed to show any appreciable response to treatment with radioactive phosphorus. Polycythemia vera frequently responds fairly well to large doses of the radioactive isotope, but judging from the case reports, the subjective improvement in these patients is considerably greater than is the hematologic response.

Sound criteria for the selection of patients who may be expected to benefit from radioactive phosphorus treatment have been formulated by investigators of the Memorial Hospital⁵⁹ and the Crocker Radiation Laboratory.⁵⁷ Proper selection of patients and careful regulation of dosage^{57, 60} will, no doubt, increase the beneficial results of this form of treatment, although it is likely that radioactive phosphorus will continue to be only a palliative agent for a relatively few types of disease.

On theoretical grounds, hyperthyroidism should be readily amenable to treatment with radioactive iodine. Iodine is localized specifically in the thyroid gland, and to a greater degree in hyperplastic thyroid tissue than in normal thyroid tissue. Its radiations are fairly destructive, and in experimental animals complete necrosis of the entire thyroid gland has been produced with radioactive iodine.⁶¹ Unlike the universally fatal disease, leukemia, hyperthyroidism is amenable to surgical treatment, and as a consequence clinical investigators have been extremely cautious in their use of radioactive iodine therapeutically, since overdosage may result in complete destruction of the gland and cause the subsequent development of myxedema. In several cases (as yet

unreported in the literature), thyrotoxic patients have been given radioactive iodine with remarkable benefit. There is every reason to believe that in the not too distant future radioactive-iodine therapy may supplant subtotal thyroidectomy in the control of hyperthyroidism.

Radioactive strontium and radioactive calcium are metabolized in similar fashion by the animal organism,⁶² and both are deposited in high concentration in the actively growing bone of osteoblastic metastatic carcinoma and osteogenic sarcoma.⁶³ The radiations of radioactive calcium are too weak to produce any therapeutic effect, but radioactive strontium emits powerful beta rays and should theoretically be of considerable value in the treatment of primary and secondary osteoblastic bone tumors. A preliminary report of the clinical use of radioactive strontium records its beneficial effect in a patient with metastatic carcinoma of the prostate.⁶³ Following intravenous injection of this substance there was cessation of pain, arrest of bone destruction and a marked drop in the serum-phosphatase level.

Six patients with osteogenic sarcoma were given injections of radioactive strontium.⁶³ The periods of observation were too short to permit adequate evaluation of the clinical effects of the therapy, but rapid and specific localization of the strontium in the actively growing tumor tissue did occur. Because of the marked radio-resistance of this type of tumor, it is doubtful whether any marked clinical benefit can be produced by this form of treatment, but it is quite probable that it will prove of some therapeutic value when used in conjunction with x-radiation.

* * *

Through the theoretically simple and technically not too difficult procedure of labeling foodstuffs, intermediary metabolic products, hormones and even tissues, it has become possible to follow the metabolic and functional interactions of these materials in normal organisms. Information so gained has completely revised many of our fundamental concepts of the biochemical and physiologic activities of living organisms. Application of this technic to the study of human disease has already provided the physician with new and effective therapeutic agents, and yet the possibilities of this technic have scarcely been realized by the majority of laboratory and clinical investigators. Extension of this method of investigation to new fields will undoubtedly yield even more fundamental and more widely practical information than has already been obtained.

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**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL**ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor***CASE 29151****PRESENTATION OF CASE**

This fifty-two-year-old Russian-born housewife entered the hospital because of a generalized skin rash.

Six months prior to admission the patient developed a pruritic, burning, red rash on the palms of the hands, which became swollen. Her physician treated her for "poison ivy" without success. Several days later the eruption became dry and exfoliative and approximately two weeks later spread to the elbow and chest. The involved skin was first red and later turned brown and resembled a sunburn. The treatment was then changed to an ointment and a "wash." At that time she became increasingly fatigued, felt feverish and could no longer do housework. She was treated with pills that may have been sulfadiazine, which she took every four hours for two days without improvement. One month later the patient was sent to a community hospital for further study. While there, her temperature ranged from 99 to 103°F., but no chills occurred. A blood study apparently ruled out pernicious anemia, and a gastrointestinal series and barium enema were negative. After five days she was discharged unimproved. By that time the skin eruption had spread to the outside of the arms and to the knees, and was dry, gray and scaly. The patient remained in bed at home because of weakness and fever, for which her physician prescribed sulfadiazine, and one month later she entered another hospital. The gastrointestinal series and barium enema were repeated, and she was told that she had an irritable colon and insufficient acid in her stomach. Treatment consisted of a liver diet and hydrochloric acid without obvious effect. During the next month she had right-sided chest pain and a chronic cough developed, which produced small amounts of white, tenacious phlegm. Because her temperature was usually about 102.5°F. she was sent to a Boston diagnostic clinic.

There the skin of the entire abdomen was described as thickened and indurated, particularly over the chest. It was reddened with a general-

ized scaly, exfoliative rash, without ulceration, that produced white silvery scales, which were consistent with psoriasis. The palms, neck, face, trunk and legs were involved in that order of severity. The throat was congested and edematous. The tongue was fissured but the papillae seemed normal; no lead or bismuth line was noted. Fine moist rales were audible at the bases of both lungs; the heart was normal. The liver was felt one fingerbreadth below the costal margin. There was no abdominal tenderness or rigidity, and no masses were felt. The temperature was 103.4°F.

Laboratory studies revealed that the urine was acid in reaction, had a specific gravity of 1.008 and gave a + test for albumin and a green sugar test; the sediment contained an occasional hyaline cast, 40 to 50 white cells and a rare red cell and an occasional squamous epithelial cell per high-power field. The red-cell count was 3,390,000 with 68 per cent hemoglobin, and the white-cell count 9300 with 55 per cent polymorphonuclear neutrophils, 23 per cent band forms, 16 per cent lymphocytes and 6 per cent monocytes. The platelets were normal in number and appearance, and there was a rare microcyte and poikilocyte. The Wassermann and Hinton tests were negative. The blood sugar was 128 mg. per 100 cc., and two days later 112 mg. The sedimentation rate was greatly increased. Cultures of the urine and blood were negative.

An x-ray film of the chest disclosed calcified nodules in the right hilar region with markedly increased markings in the middle and lower thirds of the left lung, associated with a generalized increase throughout both lungs.

Sulfadiazine therapy was begun, using 1 gm. every four hours, but since the blood level eighteen hours later was 16.5 mg. per 100 cc., the dose was reduced to 1 gm. every six hours. The urine three days later was acid and showed a ++ test for albumin and a slightly green sugar test. The sediment contained 8 white cells, 4 red cells, occasional epithelial cells and many sulfadiazine crystals per high-power field. The blood sulfadiazine level was 14.8 mg. per 100 cc., the hemoglobin 64 per cent, and the white-cell count 4800. Because of the leukopenia and the sulfadiazine crystals in the urine, the drug was discontinued.

During treatment the temperature dropped to 98.8°F., and prior to discharge the urine had a fixed specific gravity varying between 1.012 and 1.013. The patient was transferred to this hospital for further study.

The patient's mother died of cancer. One brother died of heart trouble, and another brother

er and a sister had heart trouble. The patient had had "flu" in 1918. Her last two children were not living—one died of "yellow jaundice" when eighteen days old, and the other was stillborn. An appendectomy and cholecystectomy were performed twelve years and six years prior to admission respectively. During the past year she had had irregular profuse menstrual periods associated with hot flashes.

Physical examination revealed an obese woman lying flat in bed groaning with each respiration and complaining of pain about the buttocks. The skin was generally dry and scaly and seemed atrophic, with loss of the subcutaneous fat in some places; there was a diffuse hair loss in the scalp. The face was ashen, particularly about the eyes. There were numerous thick silvery scales on the extensor surfaces of the arms and elbows, and the skin of the legs and knees was dry and covered with fine silvery scales. The palms of the hands and soles of the feet were rough, and the flexor surfaces of the fingers were fissured. There were red weeping areas on the chest and large denuded areas over each greater trochanter and over the buttocks. The tongue was very dry and covered with brownish tufts, and showed a slight coarse tremor. The cervical lymph nodes were slightly enlarged but not tender. The heart, lungs and abdomen were normal. A rectal examination was negative.

The blood pressure was 120 systolic, 88 diastolic. The temperature was 100°F., the pulse 120, and the respirations 25.

Examination of the blood revealed a red-cell count of 3,130,000 and a white-cell count of 10,500, with 59 per cent polymorphonuclear neutrophils, 11 per cent band forms, 21 per cent lymphocytes and 9 per cent monocytes. There was marked variation in the size and shape of the red cells, and a moderate hypochromia. The urine had a specific gravity of 1.008 and gave a + test for albumin; the sediment showed an occasional red cell and innumerable white cells. A phenolsulfonephthalein test was normal. The serum nonprotein nitrogen was 14 mg. per 100 cc., the sugar 108 mg., the protein 6.2 gm., the vitamin C 0.5 mg., the chloride 99.6 milliequiv. per liter, the sodium 140 milliequiv., the van den Bergh 1.2 mg. units direct (2.0 mg. indirect), and the prothrombin time 18 seconds (normal 18 seconds). A culture of the urine and a guaiac test on the stool were negative.

An x-ray film of the chest, taken with a portable machine, showed a high diaphragm on both sides, with linear areas of increased density in the left lower-lung field consistent with atelectasis.

The patient was treated with a high-vitamin,

high-calorie diet with iron supplements. Vaseline was applied to the skin, and basic fuchsin to the decubitus ulcers. The lesions improved slightly, but one week after admission the temperature and pulse rose to 103.6°F. and 120 respectively. The cough increased, and signs of consolidation developed in the left lower lobe, associated with persistent rales. Two weeks later sulfadiazine therapy was instituted, 0.5 gm. every four hours for seven doses. Suddenly, three weeks after admission, fecal incontinence developed; these stools contained large amounts of dark, clotted blood, and the bleeding continued for the next twelve hours. On the same day a large ecchymosis appeared spontaneously on the left flank. The non-protein nitrogen at that time was 22 mg. per 100 cc., the protein 4.0 gm., and the sulfadiazine level 4.1 mg. The urine was acid in reaction, had a specific gravity of 1.016 and gave a ++ test for bile; the sediment contained sulfadiazine crystals, a few cellular and granular casts and 3 white cells per high-power field. Despite blood transfusions and parenterally administered coramine, the systolic blood pressure fell to between 60 and 90 and the patient seemed to be in shock. Death occurred approximately seventeen hours after the onset of rectal bleeding.

DIFFERENTIAL DIAGNOSIS

DR. MARIAN ROPES: We had better look at the x-ray films first.

DR. LAURENCE ROBBINS: Both these films were made with a portable machine and are not particularly good. The diaphragm is elevated on both sides in the first film, and there are small localized areas that suggest atelectasis. The second film, taken several days later, shows slight increase in density and other areas that suggest atelectasis throughout the right lung field.

DR. ROPES: I do not know what this patient had, but in any case with association of extensive skin lesions, marked constitutional symptoms, renal disease, leukopenia and fever, one strongly suspects that it represents one of the many varied clinical pictures of disseminated lupus erythematosus or, possibly, dermatomyositis.

One should consider the possibility of generalized infectious disease of nonspecific etiology, such as pyogenic infection, and also tuberculous infection. But the skin lesions, clinical course and laboratory findings all seem to me to rule out, or rather not to support, such diagnoses. The generalized nature of the disease, with suggestive evidence of vascular involvement in the kidneys, raises the possibility of periarteritis nodosa, but again, the skin lesions and the absence of signs of vascular involvement in the lungs, the central

nervous system, abdomen and so forth all tend to rule it out. The initial skin lesions might be found in a case of erythema multiforme exudativum, but the subsequent progression of the lesions, the fatal course and the leukocytosis are greatly against this diagnosis.

In attempting to differentiate the two conditions that seem to be the most likely explanation of the whole picture, the predominance of skin lesions with the absence of evidence of muscle involvement is strongly in favor of lupus. We are told nothing about the muscles, but this omission itself means, I should think, that there surely was no acute inflammatory involvement, probably no marked atrophy and no obvious contracture—all of which one would expect in a severe case of dermatomyositis. Also the absence of involvement of any of the small muscles—the pharyngeal, laryngeal and ocular muscles—and the evidence of renal disease are points against dermatomyositis, as is also the presence of pleurisy, which I interpret to be the cause of the right-sided chest pain.

The entire picture, although atypical, can be explained on the basis of disseminated lupus. This disease occurs most commonly in women, usually, to be sure, at a younger age. The distribution of the skin lesions, with involvement of the palms, face and neck, is typical. The nature of the skin lesions is far from typical, however, but I do not believe they fall beyond the many varied groups that in our present state of knowledge we think are due to this disease. The cervical node enlargement was minimal and may not have been significant (it is, of course, frequently observed in cases of lupus). The relative leukopenia, with a decrease in lymphocytes and an increase in young neutrophils is entirely consistent but not diagnostic. The atrophy of the skin with marked loss of hair is also entirely consistent but not diagnostic. If the patient had had any joint pains or had had more definite evidence of pericardial, endocardial or myocardial involvement this would have been additional evidence in favor of the disease. The absence of this evidence, however, does not rule out lupus. The original chest pain, which I interpret as having been due to pleurisy, is in favor of this diagnosis. The only possible indication of sensitivity to sunlight is obtained from the fact that the first skin lesions appeared after she had been in contact with poison ivy and probably had been in the sun. That, however, is weak circumstantial evidence.

The urinary findings indicate that renal disease was present. Whether this was due to one etiologic factor or to two or three, it is impossible to say. The changes increased consistently

after each course of sulfadiazine, and the first report we have came after she had had one or two courses of sulfadiazine. It is conceivable that the kidney damage was due to the chemotherapy. On the other hand it is much more probable that it was associated with the disease, since renal damage is one of the most frequent complications of lupus. One might expect to find vascular lesions, perhaps of the so-called "wire-loop" type, in the kidneys. The terminal pneumonia is consistent with this disease, but also with any similar prolonged disease, and is in no way diagnostic.

The final episode of severe rectal bleeding is possibly connected in some way with the initial x-ray studies—the gastrointestinal series and barium enema. However, I am unable to find any reason for the two sets of x-ray studies. Also, I am unable to see why they gave the first two courses of sulfadiazine. In the absence of evidence of an infection that might be expected to respond to sulfadiazine, and in the presence of the possibility of lupus or of a similar skin lesion, sulfonamides are contraindicated because it is well known that they may cause severe and often fatal exacerbations of lupus. The final course of sulfadiazine was given in the presence of pneumonia. I still think that in the presence of lupus sulfonamides are contraindicated, but at least the indication is more apparent.

To return to the final episode—I had thought it was to be interpreted as bleeding from a severe ulcerative colitis. This does not fit in with the picture of lupus. We had one case that fell into this same general group of diseases, although Dr. Mallory was never able to include it pathologically in the group of disseminated lupus. Terminally, the patient had severe ulcerative colitis—not with massive hemorrhage but with definite bleeding. In the present case, other evidence of hemorrhage suggests that the rectal bleeding was associated with a generalized bleeding tendency. Whether this can be ascribed to liver involvement I do not know, but such a possibility is raised by the meager evidence of liver disease throughout the story. The slightly positive van den Bergh test and the palpable liver at one stage are suggestive, but the evidence is weak. I still believe that ulcerative colitis was the cause of the bleeding.

My diagnosis is disseminated lupus.

DR. ROBERT J. GLASER: I should like to ask Dr. Ropes if she considered mycosis fungoides.

DR. ROPES: I did consider it, and various other skin conditions, but I thought that it did not explain the whole picture so well as did the other diseases. The skin was the most typical part of

the whole picture and can be explained by a variety of conditions, but they do not explain the rest of the picture.

DR. AUSTIN BRUES: I saw this patient in consultation in the agonal stage and agreed with the surgeon that operation was not indicated and agreed with the house officer that transfusions should be given. By exclusion, and with considerable hesitation, I reached the diagnosis that Dr. Ropes has given.

DR. MALLORY: On reading the record, I found myself wondering whether anyone worried over the history of one jaundiced and one stillborn child to the point of suspecting that the patient was Rh negative. Apparently she was not because the transfusions were done without any reaction.

CLINICAL DIAGNOSIS

Disseminated lupus erythematosus?

DR. ROPES'S DIAGNOSIS

Disseminated lupus erythematosus.

ANATOMICAL DIAGNOSES

Acute hepatitis.

Purpura.

Gastrointestinal hemorrhage, massive.

Icterus, slight.

Neurofibroma of stomach.

Operative scar: cholecystectomy.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This is the kind of case that keeps the pathologist troubled because we have no more idea of the diagnosis after doing the autopsy than you have now, and perhaps a little less. I can only report the findings objectively.

The skin showed what is called an exfoliative dermatitis, which is certainly not a specific disease but a condition that can occur in the course of a variety of skin disorders. It occurs in psoriasis, in leukemia cutis, in mycosis fungoides and probably in lupus on occasion. I can only say that the sections show nothing to suggest psoriasis or mycosis, nothing on which a diagnosis of some underlying dermatitis can be based.

There was a severe and I think rather chronic pulmonary edema of both lower lobes. One small focus of organization was found, which suggested that there had been at least some degree of pneumonia in one of the lower lobes, but probably nothing recently acute. The heart was normal, as was the epicardium. There was a pleural effusion, but nothing that I could call a pleuritis. There were a few adhesions in the abdomen, but the patient had had a cholecystectomy.

The gastrointestinal tract was filled with blood from top to bottom. In the stomach we found a circumscribed intramural tumor, which we thought was probably a leiomyoma or neurofibroma, but the mucosa over this tumor was intact, and I do not see how it could have been the source of the hemorrhage. On the other hand the mucosa of the intestine from top to bottom was hemorrhagic, and I think this was purpuric bleeding of massive proportions. The most strikingly abnormal organ was the liver, which was greatly enlarged, extremely fatty and markedly jaundiced. Microscopically, there is acute hepatic degeneration, and I assume that the purpuric tendency was secondary to liver insufficiency. At least we have nothing else on which to explain it because the bone marrow is normal and the kidneys, so far as we can make out, are completely normal. So we are left with a variety of pathological findings that correlate with none of the clinical observations and that to my mind point to no etiologic diagnosis.

DR. ROPES: Do you remember the other case with exfoliative skin lesions and liver involvement? I wondered if she had similar liver involvement.

DR. MALLORY: She had an extremely fatty liver, with slight cirrhosis. It did not show the acute degeneration found in this case. I think most of the liver change here must have been very acute, in fact terminal, because within a week of death there was a normal prothrombin time.

CASE 29152

PRESENTATION OF CASE

A sixty-seven-year-old school principal entered the hospital because of loss of weight and strength.

Nine months before entry the patient noted the onset of nausea with occasional vomiting after breakfast. At the same time he developed a "bronchial" cough productive of small amounts of whitish nonbloody sputum. This lasted two or three weeks, and two similar episodes occurred in the two following months. The paroxysms of cough were preceded by a tickling sensation in the throat, which he attributed to a large goiter that he had had for twenty-five years. There was no dysphagia. X-ray films taken by his physician were said to have shown four small gallstones and cloudiness at the apex of the right lung. He had been taking bile salts with some relief. During the four or five months before entry he became aware of progressive loss of strength and easy fatigue not relieved by rest. His appetite was poor, and he had lost thirty-eight pounds in weight during the previous

two months. Because of midafternoon fever of 99 to 100°F., he remained in bed for the two months prior to entry. Many specimens of sputum were negative for tubercle bacilli. Three weeks before admission the patient had his first attack of rapid pulse, the rate rising to 150, with associated headache and faintness. Since then he had three similar attacks, each beginning without warning and relieved by pressure on the eyeballs or carotid sinus.

He had had left-sided pleurisy twenty-five years previously, and pneumonia on the right and a suprapubic prostatectomy five years before entry. The family history was noncontributory.

Physical examination showed a well-developed but emaciated man with a dry and pale skin. There was a large, nodular, firm, but not stony-hard, tumor of the right lobe of the thyroid gland, which extended laterally beneath the sternocleidomastoid muscle and substernally. The trachea was deviated to the left. Examination of the heart and lungs was negative. The abdomen was slightly distended; in the right upper quadrant there was a definite sense of resistance and dullness but no well-defined border could be made out. The right kidney was movable, firm, nontender and neither enlarged nor displaced; the left was not palpable. Rectal examination was negative.

The blood pressure was 100 systolic, 45 diastolic. The temperature was 100°F., the pulse 90, and the respirations 20.

Examination of the blood showed a hemoglobin of 8.2 gm. and a white-cell count of 12,100 with 81 per cent polymorphonuclear neutrophils. The urine was cloudy and amber, had a specific gravity of 1.020 and gave a ++ test for albumin; the sediment contained a few red cells and many white cells. The stools were negative. A blood Hinton test was negative. The serum nonprotein nitrogen was 23 mg. per 100 cc. A sputum examination was negative for acid-fast bacilli.

An x-ray film of the chest showed numerous areas of calcification in the left midlung field and a 1.5-cm., slightly lobulated shadow of increased density with some calcification in the region of the right middle lobe. There was scarring in the right upper lobe. A mass at the base of the right neck with calcification in its walls displaced the trachea sharply to the left and extended slightly into the chest.

By x-ray the left kidney had a normal outline. The right kidney was enlarged and there appeared to be a definite bulge with some lobulation along the lateral surface. No stones were seen. An intravenous pyelogram showed prompt excretion of the dye on the left, which outlined normal urinary

passages. The middle calyces on the right were displaced medially and showed evidence of pressure defects without invasion. A retrograde pyelogram showed only partial filling of the right middle calyx.

Cystoscopy showed only a small amount of urine in the bladder. The flow of urine was extremely slight; at first the right ureter drained hazy urine followed by very bloody urine, and the left cloudy urine.

On the seventh day the white-cell count was 31,900. The temperature fluctuated between 99 and 101.2°F. Two days later an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FLETCHER H. COLBY: It seems to me that the significant history starts with the statement that the patient became aware of progressive loss of strength and easy fatigue not relieved by rest. He also had a low-grade midafternoon fever during that time. There were episodes of rapid pulse, which I imagine were attacks of paroxysmal tachycardia associated with the enlarged thyroid gland.

On physical examination the patient gave evidence of considerable loss of weight and strength. The mass in the neck was obvious, and from the history the patient had had this mass for twenty-five years. I assume that it probably was a colloid goiter. Although there is a possibility of malignant change, the fact that the patient had had this goiter for twenty-five years makes it seem improbable. The other essential points in the physical examination are the suspicion of a mass in the right upper quadrant, the pus in the urine and the confirmation by x-ray examination that there was a mass in the right upper quadrant. X-ray examination also showed an enlarged kidney, and this is certainly better evidence of enlargement of the kidney than physical examination, because we all know how large kidneys can be and yet be missed on palpation. The intravenous pyelogram suggests trouble in the right kidney. The left kidney was interpreted as normal. This suspicion of abnormality on the right seems to be confirmed by the cystoscopic examination, when a retrograde pyelogram made of the right kidney showed that the middle calyces were displaced medially with a pressure defect and without evidence of invasion of the calyces. So I believe that the important thing to consider in this patient is the right kidney. The evidence suggests that the mass was intrinsic in the kidney itself. The kidney outline was well shown by x-ray examination and appeared to be irregular, with a definite bulge. The retrograde pyelogram indicates that this mass in-

volved the middle portion of the kidney and displaced the middle calyx. So I think the diagnosis comes down to disease within the kidney itself. The possibility of perirenal infection seems to be eliminated. This mass on the right side, presumably the right kidney, was nontender, and one would expect perirenal infection to give tenderness.

Dr. Holmes, will you be kind enough to interpret the x-ray films?

DR. GEORGE W. HOLMES: I think I had better discuss the chest film first. The mass that is described is quite evident. It lies in the upper part of the anterior mediastinum in the region of the thyroid gland and contains calcium. So the only other things we have to think of are parathyroid tumor and a calcified tuberculous node. The position is very much against the latter. The findings in the lungs are more suggestive of tuberculosis than of anything else. There is one round shadow that might be a metastasis from a tumor.

DR. COLBY: That is the one with the fairly sharp edge?

DR. HOLMES: Yes; it is not quite so dense as one would expect it to be if it were old tuberculosis.

DR. COLBY: Calcification is described in that mass. Could it not be calcification somewhere else?

DR. HOLMES: It is not impossible for a tumor to show calcification. So I cannot state whether the shadow was due to tumor or to old tuberculosis. I do not see how one can connect it with the shadow in the neck.

DR. COLBY: The calcification in the neck is probably in the thyroid or parathyroid.

DR. HOLMES: I should think that was most likely because of the position. If the calcification was in a tuberculous node, the mass ought to lie alongside the trachea or up in the neck itself.

In the abdominal films there is a definitely enlarged right-kidney shadow. The lobulation is not so evident as one might expect from reading the notes, but I think it is present. The outline of the kidney is sharp, which is against an inflammatory lesion. In an inflammatory lesion, one usually does not visualize the kidney so well. The calyces, although displaced, are not irregular, which again is against an inflammatory lesion. It apparently is deep in the substance of the kidney, so that it pushes the calyces outward, and in all probability it is some sort of tumor. I doubt that a cyst would be in this position, and I shall be surprised if it turns out to be inflammatory. The density does not give a lead.

DR. COLBY: I think it is fair to say we come to the diagnosis of an intrinsic lesion of the right kidney. This could be either inflammatory or neoplastic.

What are the possibilities of an inflammatory lesion? First of all, a cortical abscess of the kidney should be considered. This is usually associated with preceding infection, which is possible in this patient, since he had had a low-grade fever for several months. However, he should have had backache and pain and he should have had tenderness. The pyelograms in such cases vary. My experience has been that with a cortical abscess there is a definite pressure defect, either of the kidney pelvis or, more often, of the calyces themselves. The calyces are usually compressed in a somewhat orderly fashion, and one does not see the irregular defects that are apt to be associated with tumor. So I do not believe this is a cortical abscess because of the lack of tenderness, the lack of pain, the lack of backache and the pyelographic evidence.

The only other inflammatory condition I can think of as a possibility is tuberculosis. The patient's age is against tuberculosis. Patients as old as this rarely have primary renal tuberculosis unless there is a definite past history of other lesions. That does not make it impossible. However, the patient apparently had had no bladder symptoms, and an irritated bladder is the most frequent symptom of renal tuberculosis. No ulceration or inflammatory change was described in the bladder on cystoscopic examination. Furthermore, the pyelogram was not consistent with tuberculosis. One would expect to find tuberculosis in more than one portion of the kidney, and as Dr. Holmes described the pyelogram, it does not suggest an inflammatory lesion.

So far as neoplasm is concerned, what is the possibility of metastatic malignant disease? The thyroid gland might have undergone malignant change, but I do not believe so, and I am going to discount that. Primary tuberculosis of the thyroid gland is rare, and if it occurs, is usually associated with miliary disease in general. Is that not true, Dr. Holmes?

DR. HOLMES: Yes.

DR. COLBY: At the Lakeville Hospital we have had only a few patients with tuberculosis of the thyroid gland.

The possibility of primary lung tumor that metastasized to the kidney should be mentioned. However, there is no real evidence that this patient had a primary carcinoma of the lung. In addition, the other systems give no lead to a pri-

mary tumor that might have metastasized to the kidney.

So we come down to the possibility of primary malignant tumor in this patient's right kidney. He had fever, weakness and loss of strength, and in our experience at this hospital these are evidence of malignant neoplastic disease somewhere. Although there is no convincing evidence of symptoms such as pain, hematuria and tumor, which are the three cardinal signs of renal tumor, these have long since been discarded as early indications of neoplasm. I cannot explain the fever except to say that it was evidence of infection. The well-marked anemia and the white-cell count of 31,000 after cystoscopic examination could have been due to the flaring up of an already present infection in the urinary tract. The kidney outline was suggestive of neoplasm, and the pyelogram indicated a tumor that involved the middle portion of the kidney. The area in the chest might have been a secondary deposit from a tumor of the kidney.

My diagnosis is a primary malignant tumor of the right kidney; and most of these tumors are renal-cell carcinomas.

CLINICAL DIAGNOSIS

Carcinoma of kidney.

DR. COLBY'S DIAGNOSIS

Primary malignant tumor of right kidney.

ANATOMICAL DIAGNOSIS

Undifferentiated carcinoma of right kidney.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: At operation a large tumor (9 by 6 by 4 cm.) of the right kidney was found, which proved on section to involve most of the midportion of the kidney. The tumor was yellowish and necrotic, and microscopically shows an undifferentiated carcinoma, probably of embryonal origin. There was no invasion of the renal vein or pelvis, although the latter was displaced by the tumor.

DR. COLBY: Does anyone know anything about the nodule in the chest?

DR. CASTLEMAN: No. The calcification in the neck might well have been a colloid goiter; many of them have some areas of calcification.

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CANCER CONTROL IN WARTIME

THE urgency of caring for acute diseases and injuries in wartime naturally overshadows to some extent the importance of chronic diseases. Just as there has been an increase in the occurrence of pulmonary tuberculosis, there will undoubtedly be an increase in the number of advanced cases of malignant disease.

One of the unfortunate features of the shortage of physicians and nurses brought about by the war is that it becomes increasingly difficult to give the attention and study necessary for solving the difficult diagnostic problems not infrequently presented by cancer in its early stages. When, combined with this reduction in skilled personnel,

there is a consequent reduction in the special facilities for caring for cancer patients, such as that now occurring at the Westfield and Pondville state hospitals for cancer, it becomes all the more important for the general public to be aware of the signs and symptoms of at least the commoner types of early cancer.

For several years the month of April has been designated as Cancer Month by the President. That custom is being continued this year. In spite of the excellent work that has been done in public education in the field of cancer in this state for the past years, it is well to remember that the point has not yet been reached at which one can be complacent with regard to the control of this disease.

An interesting study concerning the adequacy of the general public educational program in cancer control has been made recently in Connecticut.* Among 158 successive cancer patients admitted to the New Haven Hospital, over 80 per cent had delayed in seeking or following medical advice; 60 per cent of the patients did not regard their symptoms as "serious enough" to suggest cancer. Only 11 per cent came in without delay. About 25 per cent of the patients had read about cancer and only 2 patients had ever heard a lecture on cancer. Although, in general, the group could be regarded as poorly informed, 80 per cent of them believed that cancer was curable and 90 per cent realized that, once the presence of the cancer was established, treatment was urgent.

In connection with the activities in cancer education in Massachusetts, the Division of Adult Hygiene of the Department of Public Health is conducting a survey of a modified Gallup-poll type in Malden and has completed one in Lynn to determine what the general level of knowledge of cancer is among the population. It then contemplates carrying on educational work in this field and several years later re-surveying to determine the adequacy of such a procedure. Studies of this type will aid in evaluating the efficacy of educational cancer-control measures.

*Harms, C. R., Plaut, J. A., and Oughterson, A. W. Delay in the treatment of cancer. *J. A. M. A.* 121:335-338, 1943.

OBVIOUS MEDICAL CAUSES FOR DEFERMENT

MEDICAL Circular No. 3, issued by the National Headquarters of the Selective Service System,* deserves the attention of all physicians, especially those who are engaged in the preliminary physical examinations of men prior to induction into the armed forces. The circular lists both alphabetically and by systems the defects that are "manifestly disqualifying" and gives a brief outline of the procedure required for examinations by the local boards, whose purpose is to weed out the obviously unfit, thereby saving unnecessary travel expenses and also much time at the joint Army and Navy induction stations, where a man must (with rare exceptions) be examined completely by all the specialists even though he is rejected by one. In the past, failure on the part of the examining physicians to adhere strictly to Selective Service regulations has had the result that men with such gross defects as the loss of one leg or advanced tuberculosis were occasionally sent to induction stations. This need not be. The circular points out that there are three requisites to the success of his preliminary examination: enthusiastic acceptance of the program, complete familiarity with the *revised* regulations and strict adherence thereto.

The physicians who conduct the preliminary screening do so gratis. Their only recompense is the knowledge that they are performing an extremely important function; however, as the circular points out, they do have an excellent opportunity for increasing their ability to recognize truly disqualifying defects in the brief time at their disposal. That their work is appreciated by the medical officers of the Army and Navy cannot be overemphasized.

A half-hour study of this circular should do much to increase the effectiveness of the very important screening process daily taking place throughout the country.

*Preliminary physical examination. Medical Circular No. 3, issued by National Headquarters, Selective Service System, Washington, D. C. February 15, 1943.

MEDICAL EPONYM

TRAUBE'S SEMILUNAR SPACE

Ludwig Traube's (1818-1876) observations concerning this space are available only at second hand through a communication by one of his staff assistants, Dr. Fraentzel, who published contributions from the clinic of Privy Councillor Ludwig Traube entitled, "Bemerkungen über den halbmondförmigen Raum [Observations concerning the Semilunar Space]." This appeared in the *Berliner klinische Wochenschrift* (5:509-511, 1868). A portion of the translation follows:

The fact that there is a region in the lowest part of the side of the thorax where the percussion note is tympanitic has long been recognized. Traube has made the first careful observations and investigations of this fact, the results of which may be summarized as follows:

(a) The above-mentioned region of tympany has an approximately semilunar form, that is, it is bounded below by the costal margin and above by a curved line with its concavity directed downward.

(b) This semilunar space begins anteriorly below the fifth or sixth costal cartilage and extends along the costal margin posteriorly to the anterior extremity of the ninth or tenth rib.

(c) Its greatest width is three to three and a half inches [Zoll].

(d) The note within this space, when the relation of the stomach and colon are normal, is distinguishable from the lung note above it not only by its tympanitic quality but also by its higher pitch.

(e) With deep inspiration, as the lung descends, the semilunar space is considerably diminished, and this circumstance then serves as evidence of normal mobility of the lung margin.

(f) A significant enlargement or widening, usually associated with immobility of the lower margin of the left lung, is one of the most important signs of retraction of the lung.

(g) In the presence of pleuritic exudate, the semilunar space may completely disappear, and the beginning of resorption may be first indicated by its re-appearance, and its disappearance at times may be most clearly demonstrated by the widening of the space.

(h) In the presence of pneumonic infiltration of the whole left lower lobe, the semilunar space either remains intact or is only slightly narrowed.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON INDUSTRIAL HEALTH

Some changes in the timing of the program on Industrial Health to be held at the Harvard Club in Boston on April 24 have been necessary. The corrected program is as follows:

- 9:30 Methods Used in Establishing a Diagnosis of Industrial Poisoning. Dr. Joseph C. Aub.
10:00 The Late Effects of Craniocerebral Trauma: A consideration of the criteria necessary to evaluate the possible causes. Dr. Donald Munro.

- 10:30 Medical Causes for Rejection in Selective Service. Lt. Colonel Lewis S. McQuade.
Neuropsychiatric Causes for Rejection in Selective Service. Dr. Harry C. Solomon.
- 11:15 Medical Aspects of Absenteeism in Industry. Dr. Louis R. Daniels.
- 12:30 LUNCHEON (Guest speaker: Dr. Alice Hamilton).
- 2:15 Present Status of Relation of Heart Disease to Industry. Dr. Paul D. White.
- 2:45 The Problems of Women in Industry. Dr. Thomas L. Shipman.
- 3:30 Epidemic Keratoconjunctivitis. Dr. Irving R. Tabershaw.
- 4:00 Opportunities for the Prevention and the Treatment of Diabetes in Industry. Dr. Elliott P. Joslin.
The Treatment of Trauma in Diabetic Employees. Dr. Leland S. McKittrick.
Industrial Hazards for Diabetic Employees. Dr. William A. Bishop.

DWIGHT O'HARA, *Chairman*

SECRETARY'S OFFICE

The following letter deserves close scrutiny by all members of the Massachusetts Medical Society.

MICHAEL A. TIGHE, *Secretary*

* * *

CITY OF BOSTON
VETERANS' GRAVES REGISTRATION

March 25, 1943

Dear Dr. Tighe:

Chapter 46, Section 10, of the General Laws calls for the physician, as indicated on the face of the standard certificate of death in red letters, to furnish information concerning military service, if any, on the part of the deceased.

In several certificates that have recently come into the Registry with the word "No," we have found that the deceased was a veteran, owing to the request of some party for a certified copy of the certificate.

We ask that your membership be advised of the above matter.

May I express my appreciation of your help and courtesy in the past.

Yours very sincerely,
F. W. Foss, *Supervisor*

Veterans' Graves Registration
City of Boston

DEATHS

BYRNE—CHARLES A. BYRNE, M.D., of Hatfield, died April 3. He was in his eighty-first year.

Dr. Byrne received his degree from Long Island College of Medicine in 1894. He was a member of the Massachusetts Medical Society and the American Medical Association.

DENNISON—ARCHIBALD S. DENNISON, M.D., of Lynn, died January 22. He was in his seventy-fourth year.

Dr. Dennison received his degree from the Bellevue Hospital Medical College, New York, in 1896. He was a member of the Massachusetts Medical Society, the American Medical Association and the American College of Physicians.

DWYER—PHILIP R. DWYER, M.D., of Salem, died February 28. He was in his forty-ninth year.

Dr. Dwyer received his degree from Harvard Medical School in 1920. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and a daughter survive him.

GATES—ERNEST A. GATES, M.D., of Springfield, died January 4. He was in his seventy-second year.

Dr. Gates received his degree from the Dartmouth Medical School, Hanover, New Hampshire, in 1895. He was a member of the Massachusetts Medical Society and the American Medical Association.

HENDERSON—CHARLES R. HENDERSON, M.D., of Reading, died March 31. He was in his seventy-sixth year.

Born in Hertford, England, he received his degree from Boston University School of Medicine in 1889. He was school physician in Reading for twenty years. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and a daughter survive him.

HOLMES—MAY S. HOLMES, M.D., of Orleans, died April 4. She was in her seventy-third year.

Born in Lee, she received her degree from the Woman's Medical College of the New York Infirmary for Women and Children in 1895. She was formerly superintendent of the Belmont Hospital, Worcester. She was a member of the Massachusetts Medical Society and the American Medical Association.

LOWELL—WILLIAM H. LOWELL, M.D., of Winchester, died March 31. He was in his sixty-eighth year.

Born in Halifax, N. S., he received his degree from the Harvard Medical School in 1902. He was for many years a member of the staff of the Massachusetts Eye and Ear Infirmary and was consulting surgeon to the Massachusetts General Hospital, to the Lawrence Memorial Hospital in Medford and to the Lawrence General Hospital. He was on the board of examiners of the American Board of Ophthalmology.

Dr. Lowell was a member of the Massachusetts Medical Society, the American Medical Association, the American Academy of Ophthalmology and Oto-Laryngology, the New England Ophthalmological Society and the Harvard Club of Boston.

His widow, a son and a daughter survive him.

WAR ACTIVITIES

INDUSTRIAL MEDICINE

CONTROL AND TREATMENT OF NITROUS-FUME POISONING

A conference on nitrous-fume poisoning was held in Cincinnati, Ohio, on January 28, 1943. The literature on poisoning by nitrous fumes and case histories of recent fatal and nonfatal cases of poisoning were reviewed. The suggested engineering control measures were ventilation, adequate exits and proper storage of materials likely to cause nitrous-fume exposures.

Several medical control measures were suggested:

- (1) Pre-employment examinations should include x-ray films of the chest and the exclusion from employment persons with certain upper respiratory conditions, asthma, reactivated tuberculosis and diseases of the heart.

(2) Any exposure should be reported promptly, and the worker should be referred to the hospital for an evaluation of exposure

(3) Any workers showing evidence of burning of the throat or chest, epistaxis, lassitude, pallor, cyanosis and abnormal breathing should have absolute bed rest for twenty four hours as a minimal period of observation (distressing symptoms may show up as long as seventy two hours after exposure) During the observation period the patient should be kept warm supplied with oxygen if necessary, given a liquid diet and have his blood pressure and pulse taken at regular intervals and recorded. The blood picture should also be studied periodically, particularly as regards the red-cell count and hemoglobin and methemoglobin determinations

If definite evidence is obtained that pulmonary edema is developing

- (1) Bleed the patient (500-600 cc)
 - (2) Use plasma to combat the hemoconcentration
 - (3) Administer oxygen continuously (administration under pressure may be advisable)
 - (4) Do not give morphine, if sedation is necessary, Allonal or luminal should be used
 - (5) Use of cardiac stimulants should be discouraged
 - (6) As this is an uncompensated alkalosis, soda is contraindicated
 - (7) Give concentrated glucose intravenously
 - (8) Mercury diuretics may be tried
 - (9) Adrenocortical hormones may be tried
 - (10) The most satisfactory treatment is prevention
- Reprinted from *Industrial Hygiene*, a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service

MISCELLANY

GRADUATION AT TUFTS

A total of 94 men and women were graduated by the Tufts College Medical School at convocation ceremonies held jointly with Tufts College Dental School on Sunday afternoon, March 28, in the Cousens Gymnasium on the Medford campus. Three of the ten medical students graduating with honors are residents of Metropolitan Boston. Elliott Bresnick, of Brookline, Lawrence F. Cozza, of Somerville, and George L. Cushman, of Medford. In addition to being the first convocation of degrees held since the war accelerated training program was adopted a year ago, the exercises were the first that the two schools have held separately from the other schools of Tufts College.

Honorary degrees were awarded to three physicians. The degree of Doctor of Laws was conferred on Dr. Lewis H. Weed, professor of anatomy at Johns Hopkins University School of Medicine, and chairman of the Division of Medical Sciences, National Research Council, who delivered the convocation address, "War Research in Medicine and Dentistry." The degree of Doctor of Science was awarded to two alumni of Tufts College Medical School. Commander A. Warren Stearns, USNR, dean of the school, who is now in active service, and Dr. Frank R. Ober, Dr. Lee S. McCollister, chaplain emeritus of Tufts College, gave the prayer and benediction.

REPORT OF MEETING

GREATER BOSTON MEDICAL SOCIETY

A regular meeting of the Greater Boston Medical Society was held at the Beth Israel Hospital on November 11, 1942, with Dr. Hyman Green presiding. Dr. Joseph C. Aub spoke on the topic *The Present Status of Hormone Therapy* making special reference to the role of testosterone and diethylstilbestrol.

It was emphasized that the mode of action of many of the hormone products is not understood, and that what is known is based largely on evidence gleaned from urinary assays. But a low assay may be interpreted in a variety of ways, for instance as a greater breakdown in the body before secretion, or as a diminished secretion.

Testosterone was isolated in 1934 and crystallized the following year. It has been found to be ten to twenty five times more potent than other androgenic substances. The effect of this, like that of other hormones, is greater when there is a definite lack in a patient. The best index of activity is the effect on children. This substance causes a marked increase in the size of the penis or clitoris, including as well as of the prostate and the seminal vesicles in boys and a development of all secondary sex characteristics. The results are dramatic in the eunuch, in whom the deficiency is outspoken. Such patients should receive 25 mg intramuscularly three times a week or 10 to 20 mg of the methyl salt daily by mouth. The deepening of the voice that may occur sometimes alarms girls but is usually a reversible change, which can be rectified by withdrawal of the drug. There may also be hirsutism with male distribution, as well as an increase in musculature and a swing toward a male type of habitus. All these effects are apparently greater following the intramuscular use of the hormone. In those lacking the hormone, such as eunuchs, there is generally a feeling of well being, with aggressiveness and increased libido. It should be noted that the use of testosterone also affects other internal organs, as evidenced by an increase in size of the kidneys and so forth. In all these hormonal appraisals the balance between the male and female factor is probably more significant than the absolute amount of either. For example, those with Frohlich's syndrome may excrete large amounts of ketosterones and have high estrogen values as well.

Testosterone has a definite effect on skeletal growth and epiphyseal closure. There is great stimulus to growth, especially in undersized children, and at the moment, it is the best available material for this purpose. The increase in secondary sex characteristics limits the amount of therapy that can be given. The two important factors are growth and maturation. No stimulus is of much value if it increases the closure of epiphyses at the same or a faster rate than it stimulates growth. But it is thought that testosterone, unlike desoxycorticosterone, increases the bone age little if any and is therefore superior as a therapeutic agent in stunted growth of endocrine etiology. Oral methyl testosterone is satisfactory for this purpose in daily doses of 10 to 20 mg. The appearance of secondary signs is less of a problem, but one should watch for evidence of hirsutism and change of voice. Although the hair usually disappears with withdrawal, the change of voice is often permanent.

Knowledge of the growth mechanism has been obtained from a study of deer antlers. In this animal there is only one cycle, the testes being quiescent from December to June, followed by activity associated with tremendous

antler growth. The rate of growth far outstrips any known tumor, and there is associated growth of all other sex characteristics. Although the local phosphatase values are high at the antler tip, there is no change in the serum phosphorus, calcium or phosphatase, unlike cases of osteogenic sarcoma. The antlers start their growth at least one month before any change in the testes, and growth stops when the testes atrophy. Castration when the antlers are well developed causes them to drop off soon; whereas the same procedure at an early period results in a slow, gradual increase in their size over the entire year. The latter never drop off. The impetus probably arises in the anterior portion of the pituitary gland, as evidenced by growth of the antlers before the testes. No change in the thyroid or adrenal gland has been noted at any time.

The use of testosterone in women has led to many controversies. The importance of the ketosteroid-estrogen relation was again stressed. There seems to be some effect on libido, whereas there is definite improvement in certain cases of endometriosis and questionable benefit in patients with uterine fibroids. In normal women, menstruation may be suppressed for several months if enough is given. This is probably a secondary effect through the pituitary gland. This disturbs the ovarian cycle. One of the most practical uses of the drug is in reducing mastodynia and premenstrual stress. At the menopause, it is apparently as effective as the estrogens, although the mechanism has as yet not been established. The pruritus and eczema of this trying period also seem to be benefited.

Diethylstilbestrol, although it is chemically not a true estrogen, has the same physiologic effects. However, it is also a more potent carcinogenic agent and should therefore be used with caution. It is not a substitute for the estrogens but is interchangeable with them, at least at the menopause. The disadvantages are occasional nausea and skin lesions, such as pruritus and a macular rash. A few patients exhibit evidence of allergy although they have never before had the drug. There have been no serious sequelae. A good indication of sufficient hormone is the onset of mammary enlargement in either sex, with some discomfort and tingling. This may even occur in children in whom the drug is being used for the treatment of vulvovaginitis. The breast enlargement seems to be ductile and periductile rather than acinar. The drug is certainly a satisfactory hormone, and many of the objections to it seem unfounded. Doses of 0.5 to 1.0 mg. daily by mouth seem innocuous from the standpoint of carcinogenesis. It is much cheaper than the estrogens. End-result studies are not yet available, however.

The anterior portion of the pituitary gland is probably the stimulator of the above-mentioned organs, and its substance would therefore be the drug of choice. But there are as yet no potent nor proved preparations from

this master gland. Therefore, treatment is now of a substitute variety. One of the main faults with such therapy is that the secondary sex characteristics are stimulated without any effect on the sex organs or their secretions. The latter may even be decreased.

The discussion was started by Dr. Harry B. Friedgood. Testosterone treatment of youngsters should still be confined to physicians who are acquainted with the physiology of the substance, since there may be untoward effects. There is no question that this substance does cause descent of the testicle and bone growth. Testosterone in the management of eunuchs is remarkable: it improves their emotional stability and decreases their tendency for infection of all sorts. It is believed that oral methyl testosterone is as satisfactory as testosterone from the point of results and is somewhat safer. There should be some hesitation in the use of this hormone in girls and women because of its ill-effects. Hypertrophy of the clitoris may remain as well as a permanent change of voice, and hirsutism only recedes slowly. If employed the patient should be followed with vaginal smears and all manifestations should be closely checked.

Dr. Friedgood is reticent about using diethylstilbestrol because of its lack of chemical similarity to the estrogens. Furthermore, the short duration of untoward symptoms does not rule out a toxic effect. The end results on the score are still to be recorded, and there have been reports of toxic changes of the liver and kidneys.

Dr. Samuel Gargill emphasized the efficacy of testosterone as a substitute for the estrogens in certain conditions. He has been impressed with the superior quality of the methyl derivative for growth stimulus and also the control of functional uterine bleeding. Diethylstilbestrol has been used for four years with few reactions. It has been especially effective at the menopause. Ethanol estradiol competes in cheapness and is good in small doses, but there are still some toxic manifestations.

Dr. Henry Finkel spoke about the efficacy of progesterone in the treatment of habitual or threatened abortion. This procedure is based on the theory that there is in such women a deficiency of this hormone, which is thought to be responsible for proper implantation of the ovum and for a decrease of uterine contractions. Of course, in abortions the fetus has been dead for several weeks and in such cases there is actual harm in prescribing the hormone, because of the danger of malignant degeneration in a retained fetus. Therefore, progesterone should be administered post conception in suspected cases, and even then it will be of avail only if there is a progesterone deficiency and all other conditions are normal.

In conclusion, Dr. Aub warned against the dangers inherent in these preparations, which will be enhanced with further purification of the hormones. All those planning to employ them should be acquainted with the proper dosage and the side effects.

(Notices on page xii)

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SIGNIFICANCE OF SYSTOLIC CARDIAC MURMURS IN COLLEGE STUDENTS¹

ANDREW W. CONTRATTO, M.D.[†]

BOSTON

AS ONE becomes interested in heart disease the many problems connected with the cardiac status among young people demand attention. Questions frequently arise concerning young persons that do not occur so often in older age groups. Many times one is faced by the question of how to interpret a heart murmur. Does it or does it not mean organic heart disease? If it does, what type of restrictions are demanded and what sort of life should this person lead?

If one is to avoid injustice and serious injury to the future of these young people he must carefully weigh all the evidence before making a diagnosis of organic heart disease. With the increasing interest in matters pertaining to health such as high school and college physical examinations, industrial health requirements and more particularly Selective Service examinations, more and more problems concerning the interpretation of cardiac findings are sure to arise. A rational attitude toward these findings must be assumed. Certainly it is a greater error to make the diagnosis of an organic heart lesion in a person with a normal heart than it is to make one of a normal heart in a person with a minimal valve lesion without any other cardiac finding. In the first case, not only is the way paved for the making of a cardiac neurotic but also the course of an otherwise normal life may be changed to one that becomes a burden to the patient and to society. On the other hand, the amount of damage done to a heart with minimal valve lesions and no evidence of active rheumatic fever is probably nil under ordinary physical strain.

The physical sign that causes the most difficulty in evaluating the cardiac status of a young person is the systolic murmur. The exact mechanism involved in the production of such mur-

murs is not understood. It may be assumed that a good many of them are due to stenosis of the various heart valves, namely, aortic pulmonary or tricuspid stenosis. Likewise, congenital defects may be responsible. In many cases the murmur may be due to hypertension or to arteriosclerosis dilatation, or atheroma of the aorta without valvular lesions. One not infrequently hears a very loud systolic murmur all over the precordium, in some cases with a pronounced thrill, and discovers perfectly normal heart valves at autopsy, so that no satisfactory explanation of the murmur is found. If this is true of pronounced systolic murmurs a murmur of much less intensity must be interpreted with even greater caution as meaning organic heart disease. Most examiners interpret as functional all systolic murmurs over the pulmonic area of Grade 2 or less.¹ In addition, many physicians disregard soft systolic murmurs over other parts of the precordium, provided no other signs or symptoms of heart disease are present. However, in routine examinations one frequently hears a systolic murmur that because of its intensity, location and so forth causes concern. In this study an attempt was made to evaluate systolic murmurs in young people.

MATERIAL AND METHOD OF STUDY

The Department of Hygiene at Harvard University has afforded the opportunity to make a study of the cardiac status of youths in their late teens who represent a good cross section of native Americans, both socially and geographically, although probably on a higher economic level than the average youth. Through this department, each Harvard freshman is required to have a routine physical examination by specially qualified physicians. Before the student appears for examination, as much information as possible about his previous health is obtained from the parents. A detailed history is then elicited by the examiner.

[†]From the Department of Hygiene, Harvard University.
¹For statement on medicine Harvard Medical School as on a late Professor Benjamin Chambliss, Boston physician Department of Hygiene Harvard University.

The following points in the cardiac examination are stressed: a possible history of rheumatic fever or any known form of heart disease; any past restrictions in physical activities because of "heart trouble"; the size of the heart and the rate, rhythm and blood pressure; the presence or absence of murmurs and, if present, the area where best heard and the kind and intensity of the murmur.

The first group selected for this study was the Class of 1941, numbering 946 students; the second group was the Class of 1942, numbering 938 students; and the third group was the Class of 1943, numbering 972 students. This made a total of 2856 students examined.

RESULTS

Incidence of Rheumatic Fever

Of these 2856 subjects, a definite history of rheumatic fever was obtained in only 13 cases, or less than 0.5 per cent of the total group. In addition, 1 student developed rheumatic fever for the first time while attending college. This low incidence of previous rheumatic fever is noteworthy, especially since a fair number of the students were born and reared in the region of the northern Atlantic seaboard.

Careful examination of the group with a previous history of rheumatic fever showed no cardiac murmur whatsoever in 5. Five subjects had systolic murmurs that were barely audible and confined solely to the pulmonic area; 2 had definite evidence of valvular heart disease, and 1 was classified as having possible mitral stenosis.

Spurious Heart Disease

The most interesting and important group consisted of 26 students who, previous to entering college, had been restricted in physical activity because of so-called "heart disease." The majority of the cases were brought to attention by letters from the family before the students appeared for routine examination. These letters usually contained statements that the youth in question had a "bad heart" and must be careful not to over-exert himself. In most cases, so far as could be learned, the diagnosis of "heart trouble" had been made years before by the family doctor, usually because of the presence of a systolic murmur. Among these 26 students in 7 no murmur whatsoever was heard, nor were there any other abnormal cardiac physical signs. Three of the 7 had a previous history of rheumatic fever. Fourteen students had only a very soft systolic murmur at the base or apex, without any other evidence of heart disease. One had benign extrasystoles. Two had evidence of active rheumatic heart disease with valvular lesions, and 2 had the

physical findings of congenital heart disease. Thus, only 4 of the 26, or 15 per cent, had organic heart disease. On the other hand, 22 (85 per cent), on the most careful examination, including 7-foot heart films and electrocardiograms in the doubtful cases, were found to have no heart disease. Thus it seems that a great many young persons are classified as having organic heart disease when it does not exist. Moreover, these young men are unnecessarily restricted from the usual activities of their age. This is certainly not conducive to good physical and mental health, and in some cases the personality is definitely warped. On the other hand, it should be remembered that youths who have had rheumatic fever and previous evidence of acute or subacute myocarditis may give no indication of organic heart disease at some subsequent examination.

Systolic Murmurs

In the entire group of 2856 students, a systolic murmur of some degree was heard in 350 cases (12.3 per cent). In 208 (7.3 per cent of the total), the murmurs were of such character and intensity that they were classified as functional by the examiner, and the subjects were therefore dismissed as having normal hearts. In 9 cases (0.3 per cent of the total) the cardiac findings led to a positive diagnosis of inactive rheumatic heart disease with valvular lesions. Six (0.2 per cent) had congenital lesions. The remaining 127 subjects (4.6 per cent of the total) had systolic murmurs of such intensity and location that they were not classified as functional, nor were the findings sufficient to make possible a diagnosis of organic heart disease.

It is in the last type of person that careful study, history-taking and intelligent interpretation of the findings are necessary if one is to avoid error. In order that as much information as possible might be obtained for this purpose, all these students were subsequently seen and examined by me and followed at regular intervals. The cardiac examination consisted of heart size, rhythm, rate, blood pressure, character and intensity of murmur and the area in which it was best heard. The examination was made with the patient lying on his back, on his left side, sitting and after exercise. The intensity of the murmur and the area in which it was best heard were recorded according to the method of Freeman and Levine.¹ In all cases where there was doubt as to cardiac size, a 7-foot heart film was taken. Likewise, if there was any disturbance of rhythm, an electrocardiogram was taken. In no case was any abnormality found in either the heart film or the electrocardiogram. The majority of these students were fol-

lowed at six-month intervals, with a cardiac examination at the end of each period. Thus, it was possible to follow the group from the Class of 1941 for four years, that from the Class of 1942 for three years, and that from the Class of 1943 for two years.

In analyzing these cases, it was found that the systolic murmur was most pronounced at the pulmonic area in 50 per cent of the cases and at the apex in 39 per cent, and was of equal intensity in both places in 11 per cent. The murmur was invariably intensified after exercise, with an increase in heart rate. Likewise, in most cases the murmur was more pronounced in the supine than in the sitting position. However, the position, the area in which the murmur was best heard and its relation to exercise were not enlightening concerning whether the murmur was organic.

These students were allowed unrestricted activities, and during the follow-up study no noticeable change in cardiac findings occurred. Moreover, in no case was a diagnosis of valvular heart disease subsequently made.

SYSTOLIC MURMURS AND EXERCISE

As stated previously, none of the students with systolic murmurs alone were restricted in exercise. However, one is frequently forced to make decisions concerning how much and what kind of exercise and so forth are to be permitted when a student has an unusual cardiac finding. This is illustrated in the following two cases.

G. H., aged 19, had rheumatic fever three times in childhood, the last attack at the age of 13. He was thoroughly studied at the Presbyterian Hospital, New York City, in 1932, at which time all the studies were normal with the exception of a moderately rough, Grade 2 systolic murmur over the precordium, best heard at the apex. No diastolic murmur was heard. In 1937, when he reported as a freshman, the same cardiac findings were present. There had been no intervening history of rheumatic fever. Fluoroscopic examination of the heart was normal in all respects. The white-cell count and sedimentation rate were normal, and so far as we were able to ascertain, there was no difference in the heart findings in 1937 and those of the previous 5 years. The student was eager to be allowed to play football. This was permitted, with the understanding that he would report at least twice a year for a cardiac check-up. During his 4 years in college he played freshman and varsity football. At no time was there any change in the cardiac findings, nor were there any evidences of smoldering rheumatic infection.

L. M., aged 18, had a negative past history, with no evidence of rheumatic fever or chorea. He had always been active in sports, and played football and basketball in high school. During his routine physical examination the heart seemed clinically enlarged, the rate was slow (68), and the blood pressure was 110/70. There was a marked

sinus arrhythmia, and a rough, Grade 2+ systolic murmur was audible over the precordium, best heard over the pulmonic area. No diastolic murmur was heard. Fluoroscopy and a 7-foot heart film showed no enlargement and no abnormality in contour. Electrocardiograms were also normal. This student was eager to play football. He was allowed to do so, but his cardiac status was closely followed. A recent complete cardiac examination, including fluoroscopy and x-ray, showed no change since the original examination 3 years before.

It is my opinion that playing football has not injured either of these students, nor has it caused any progression in their cardiac ailments.

SUMMARY

The cardiac status of 2856 Harvard College students was evaluated as accurately as possible by a careful history and physical examination. When indicated, fluoroscopy, electrocardiograms and follow-up studies were done.

Three hundred and fifty (12.3 per cent) of the total group were found to have a systolic murmur. In 208 (7 per cent) the murmur was classified as functional at the time of the original examination and the cases were not studied further. In only 9 cases was it possible to make a diagnosis of inactive rheumatic heart disease with valvular lesions. In 6 cases a diagnosis of congenital heart disease was made.

One hundred and twenty-seven students (4 per cent) had systolic murmurs of such intensity or character that the original examiner was unwilling to diagnose them as functional. A good many of these subjects were carefully studied and followed for two to four years, and in no case was it possible to make a diagnosis of organic heart disease, although such, of course, may have been present.

A fairly large number of boys were studied who had previously been restricted in their activities because of heart disease that did not exist.

In 2 cases the relation between exercise and "heart murmurs" is discussed in some detail.

CONCLUSIONS

The incidence of previous rheumatic fever and inactive rheumatic heart disease among Harvard College students is very low.

Apparently, the diagnosis of organic heart disease is made too frequently when it does not exist.

Likewise, the restrictions placed on persons with minor valve deformities is probably too rigid, and may inhibit an otherwise normal program, both physical and mental.

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DEATH FROM ALLERGIC SHOCK*

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IT IS the purpose of this paper to consider a recent case of a fatality following the intradermal administration of a minute amount of foreign-proteid material, investigation of which revealed a hereditary relation to an earlier case, the history of which is drawn from the literature. As other factors in the case histories must be interpreted against the patients' common heritage, it is thought that together they may contribute evidence of value to students of atopic allergy.

Moreover, such accidents, though rare, are now largely avoidable if the parenteral administration of foreign-proteid matter is preceded by adequate history-taking, careful tests and thorough physical examination, and if, when attempted, it is discreetly done with appropriate remedies at hand to combat reactions. Not one but all these precautions constitute the "due care" imposed on the practitioner legally as well as ethically.

In Massachusetts, such fatalities come under the jurisdiction of the medical examiner. It was such an investigation in line of duty that developed the facts that this paper sets forth. In a previous communication¹ use has been made of special features of the investigation of interest to pathologists and immunologists. In this one an attempt is made to develop such features as may bear on the work and responsibilities of the clinician.

On August 27, 1940, the medical examiner of Worcester County received a call from a hospital for the insane, where an accident had occurred incident to a carefully planned research designed to determine the rate of cutaneous color-spread among schizophrenics as compared with normal persons. A physician had assembled a group of young women from among the employees. The nature of the investigation was explained to them and a fee was allotted to each. No danger was anticipated, but all the subjects were questioned concerning allergic sensitiveness and previous immunizations, to which negative replies were made in all cases. Physical examinations and eye and scratch tests had not been made, since they were not thought necessary. The test solution was guinea-pig hemoglobin, selected because of its known low antigenic power. The hemoglobin was dissolved in physiologic saline solution and made up to a

volume equivalent to that of the quantity of blood from which the corpuscles were originally derived. Only 0.2 cc. was given intradermally, a dose no greater than is often used clinically for sensitivity tests.

As the seventh subject was being injected, the fifth subject, A. D., a well-developed woman of 22, experienced respiratory distress and became cyanotic. The physician gave adrenalin and proceeded with his injections. The woman's condition soon became alarming. Adrenalin was injected into the heart and artificial respiration was applied, but to no avail, and the subject expired 10 minutes after receiving the injection.

The following is abstracted from the official report of the medicolegal investigation:

I viewed the body as it lay clothed on the bed in the room where the testing had been done. None of the other young women who had received the test were feeling any ill effects. I examined the arm of one of them and saw a puncture mark surrounded by a brownish zone about 0.6 cm. in diameter, which in turn was surrounded by a narrow zone of edema. This was similar to though less intense than that on the dead woman's arm.

In view of the seriousness and exceptional circumstances of the case, I felt that the official participants and witnesses to an autopsy prescribed by statute should be competent persons not connected with the institution. I therefore invited Dr. Alan R. Moritz, professor of legal medicine at Harvard Medical School, to co-operate with me in the autopsy. He and his associate, Dr. Herbert Lund, arrived at 5:00 p.m. The hospital facilities were placed at our disposal by the acting superintendent, Dr. William E. Barton.

The autopsy was begun about 5:30 p.m., Drs. Hunt, Moritz, Lund and Freeman participating.

The details of the post-mortem examination appear in the previous publication.¹ In summary, it revealed acute hemorrhagic inflammatory reaction at the site of a needle-puncture wound in the skin of the right forearm; edema of the mucosa of the air passages; mild laryngitis, tracheitis, bronchitis and pneumonitis; marked emphysema of both lungs, with the formation of large air-filled subpleural bullae; rheumatic carditis with mitral, aortic and tricuspid valvulitis (old); moderate arterial hypoplasia; and noninvolution of the thymus gland.

Despite the fact that sensitivity to guinea-pig protein is not common and that the dose given was extremely small, it was thought that the most tenable explanation of the fatal collapse was al-

*Read, in part, at the annual meeting of the Massachusetts Medico-Legal Society, Boston, May 26, 1942.

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lergic shock. Although it seemed possible that inflammation of the respiratory passages and chronic rheumatic heart disease may have contributed to the death, they did not in themselves provide an adequate explanation. It seemed highly desirable to demonstrate whether or not there was present

jection of guinea-pig hemoglobin. An accident of medical research. . . . Investigation failed to discover evidence of any illegal act and further judicial inquiry is unnecessary."

Although this report concluded the official investigation, other aspects of the case were in-

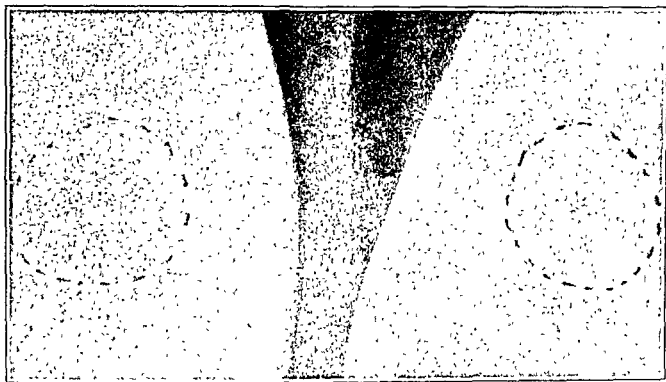


FIGURE 1. *Prausnitz-Küstner Reaction.*

The positive reaction is on the left, and the negative control on the right.

in the blood a specific reagin to guinea-pig hemoglobin. To determine this point, it was decided to employ the method of local passive sensitization.

Accordingly, 20 cc. of blood was drawn aseptically from the right auricle, and with it Prausnitz-Küstner tests were carried out on 3 subjects by Dr. Lund in Dr. Moritz's laboratory.* A detailed report of the tests appears in the paper by Lund and Hunt referred to above. They were positive in 2 subjects, but the third proved nonreactive. Figure 1 shows the intensity of the reaction in comparison with the control as both appeared on the first subject (Lund). All the controls were negative. At a later date the sensitized area was tested to mixed duck, chicken and goose feathers, with negative results. The reaction to horse dander was also negative, but dog hair gave a positive reaction. This was confirmed some weeks later when an accidental scratch by a dog on the sensitized area was followed by a large wheal. The conclusion that A.D.'s blood contained reagins specific to guinea-pig hemoglobin and to dog hair therefore seemed to be justified.

As a result of the history, post-mortem examination and passive-transfer test, the cause and manner of death were officially returned as follows: "Anaphylactic shock following an intradermal in-

triguing. From the woman's mother, hospital records and physicians under whose care A. D. had been, the following information was obtained. She had suffered from asthma for eight years and had shown positive cutaneous reactions to dog hair, kapok, shellfish, ragweed, timothy, orris root and house dust. Negative results were obtained with egg, milk, rabbit hair and chicken feathers. To her mother's knowledge the woman had never had any contact with guinea pigs. She had had symptoms in childhood that suggested rheumatic fever or infantile paralysis to the attending physicians. She had some physical signs interpreted as mitral stenosis, but there was no history of cardiac decompensation. She was a liberal but not excessive salt-eater, which would seem to rule out adrenal insufficiency.

The family history is extremely important. The mother had asthmatic attacks and symptoms of hay fever during one summer. A brother was subject to hay fever and a sister to acne. Two other sisters were normal. The brother was the only male of either the mother's or the father's line known to have been allergic. *A first cousin of the mother died in convulsions at the age of sixteen, ten minutes after a subcutaneous injection of diphtheria antitoxin.*

This patient, B.V., was also asthmatic. Her accidental death in Brooklyn, New York, in 1895

*I am indebted to these men, and accord them full credit for this ingenious application of a biologic test to the technic of post-mortem investigation.

was the first in this country to result from an injection of diphtheria antitoxin.

The story is graphically told by her physician, Dr. James L. Kortright,² as follows:

On March 27, 1895, I was called to a little boy . . . almost moribund with malignant diphtheria. The family had not suspected the serious nature of his illness and had tried home remedies for five days before seeking professional help. He died the same day. When I announced the diagnosis, his cousin, a stout,

in its course transfixes a small vein in the abdominal fat. The brain and meninges are congested. The liver, and especially the kidneys, are markedly congested. The lungs are normal. The heart is systolic; its left side is empty; the right side contains a small amount of fluid blood. There is slight atheroma of the aorta near the valves. The pulmonary artery contains no clots, and the larynx and trachea contain no foreign body.

As indicated by the photographic reproductions from the newspapers of the two periods (Fig. 2),

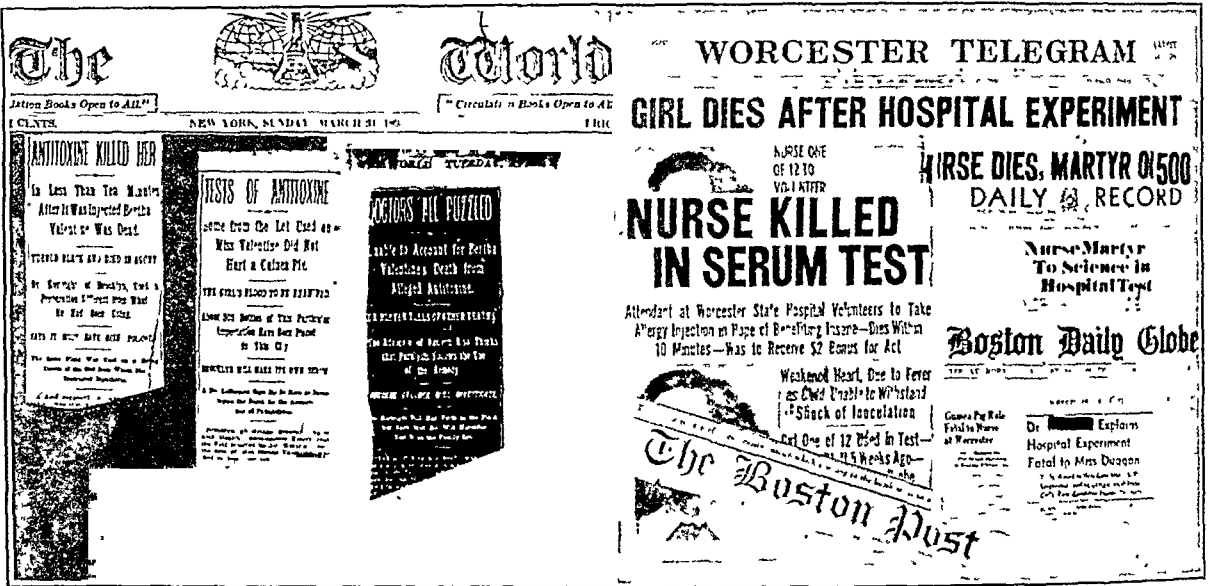


FIGURE 2.

well-nourished girl of sixteen [seventeen] years, asked me to examine her throat. There were a few spots occupying the crypts of the right tonsil. . . . On March 28 the temperature was 101°F. Nausea was present and there was a grayish exudate over both tonsils, extending upward to the pillars of the fauces and backward upon the pharyngeal wall. Bacteriological examination showed almost a pure culture of Klebs-Loeffler bacillus. At 3 p.m. of the same day she received 10 cc. of Behring's serum No. 2. The injection was made at the left lateral aspect of the abdomen. . . . About five minutes after the injection, the girl complained of tingling and became restless. . . . This paraesthesia was immediately followed by a slight general convulsion. This mild spasm was followed at once by general tonic and clonic convulsions, accompanied by marked opisthotonos, cyanosis and absolute cessation of breathing. The pulse was rapid, small and forcible. . . . Artificial respiration was kept up until the heart stopped. The time in all was perhaps three minutes from the first sensation of tingling till death.

each of these episodes created no small sensation in its respective community.

Both these patients stemmed from the same ancestry. The family has been traced to the be-

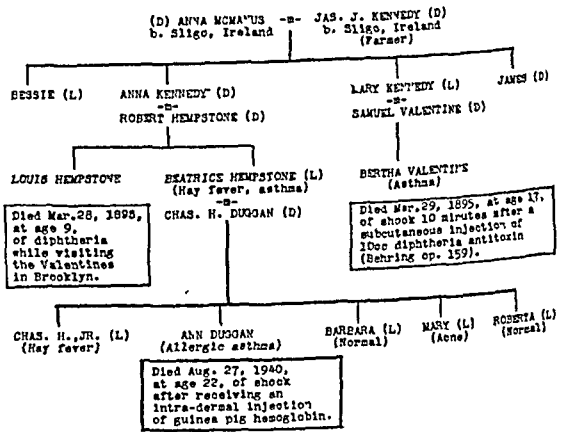


FIGURE 3.

An autopsy was performed eighteen hours after death by a coroner's physician, Dr. J. M. Clayland, whose report stated:

Body well nourished. Rigor mortis well-marked. No oedema. There is a small punctured wound on the left side of the anterior abdominal wall. This puncture does not penetrate the peritoneal cavity, but

ginning of the line on this side of the ocean and the relationships are shown in Figure 3.

The coincidence of two accidental deaths from allergic shock of young women in successive generations, although of divergent lines of the same

family, is so far as I know, unique in medical annals.

A detailed consideration of the influence of heredity in relation to allergy is beyond the scope of his paper. The cases reported here certainly show evidence of heredity sensitivity of high degree, transmitted through the females. The inheritance seemingly was not sensitiveness to species-specific antigens, unless a common antigenic fraction in horse, dog and guinea-pig proteins analogous to the Forssman heterophile antigen exists. A.D. had been shown to react to a variety of substances, and the passive-transfer test proved that she harbored reagins to both guinea-pig hemoglobin and dog hair but not to horse dander, while B.V.'s death was due to horse serum. The former had had definite exposure to a dog and her asthma had been greatly ameliorated by disposal of her pet Pekingese. But she had had no known contact with guinea pigs. It might therefore seem that she inherited a specific sensitivity as well as the capacity to become sensitized. Unfortunate for this as evidence is the probability that she had opportunities for sensitization to a guinea pig which would not necessarily have come to the knowledge of her relatives or even have been remembered by herself. It is thought that the evidence of these cases at least adds further support to the recognition of atopic persons as a distinct group in which a hereditary abnormality is the essential factor, and in which exposure to exciting substances is of secondary importance but determines the specificity of the antibodies (reagins) developed.

From the standpoint of liability to fatal reaction, A.D.'s case raises atopic hypersensitiveness to proteins of small animals to a clinical importance hitherto accorded to asthma and hay fever induced by contact with horses.

Sudden death as well as lesser effects, such as respiratory distress, collapse, pyrexia and local manifestations, including urticaria, hay fever and asthma, hypothetically result from the release of a physical irritant or a chemical poison produced by the clash (union) of antigen with antibody within the tissues of the body. That these toxic substances are of the nature of histamine is assumed by some, but their identity is as yet unknown. It is, however, well established that two definite effects, whatever the exact cause, are produced: smooth muscle is thrown into spasm, and permeability of the capillary walls is increased. These effects vary in promptness, severity and distribution according to various factors—dosage, time in relation to sensitization, the organ or tissue of the particular person in which antibodies prod

inate (individual shock organ) and, possibly, endocrine factors not yet identified but in which the thymus, lymphoid structures and adrenal cortex are under suspicion.

As in the case of other poisons that act with great speed or kill by altered physiologic functioning rather than by producing tangible structural lesions, the post-mortem findings are meager and not distinctive.

Evidence of smooth-muscle spasm may be furnished in the lung by overdistention of the air cells, often with breakdown of the alveolar walls. Such emphysematous lungs do not collapse when the chest wall is opened, but they do so slowly when incised. They are usually pale. The right side of the heart is usually distended and venous engorgement of the viscera is the rule. If death has not been too rapid, evidence of permeability of the capillaries may be shown by edema of the glottis and bronchial mucosa. Since death is asphyxial, subserous petechial hemorrhages are fairly frequent. Engorgement of the liver and portal system may be the outstanding feature. The lymphoid structures may be enlarged. The blood is fluid, and eosinophilia may be noted. Evidence of the "thymolymphatic constitution" such as characteristic bodily contours, abnormalities of thymus gland, and hypoplasia of the vascular system and adrenals may be seen. Hyperplasia of the germinal centers in the spleen and lymph nodes should be noted and checked by microscopic study. Finally, passive-transfer tests may determine the presence of specific reagins.

For establishment of a diagnosis of death from allergic shock the following criteria should, in my opinion, be fulfilled: there must be a definite history or tangible evidence of death in relation to the injection of an antigenic substance; the post-mortem findings must be consistent with death of this type, and exclude other adequate causes; antibodies or reagins specific to the substance known to have been injected must be demonstrated in the blood or tissues of the subject, or some clinical manifestation of an allergic reaction must have preceded death. A family or personal history of hypersensitiveness, if obtained, is pertinent and important but not essential.

The outstanding lesson of clinical importance to be derived from these cases is that of the ever-present danger attendant on the parenteral injection of any foreign proteid by an atopic person. Proteids capable of inducing fatal allergic shock are not limited to those derived from the animal kingdom. Lamson³ has reported a fatality following the intradermal administration of 0.05 cc. of a 1:100 solution of extract of *Bermuda grass*

and another from an intradermal skin test with a 1:500 solution of buckwheat extract, both in adults. Ziskind and Schattenberg⁴ reported a fatality in an adult Negro woman from 0.2 cc. of antityphoid vaccine given intravenously to induce a nonspecific reaction in the hope of benefiting her arthritis. A first dose of 0.08 cc. four days previously had been given without reaction.

It is startling indeed that so minute a dose of foreign matter as was given in the first case, introduced barely under the epidermis of a seemingly healthy adult weighing 135 pounds, should have resulted in immediate death. Such an occurrence is not, however, without precedent, as the foregoing examples show. Cooke⁵ in 1922 reported the death of a boy of three from a reaction to a skin test with a solution of glue. Lamson⁶ in 1924 reported the case of a child with eczema who died two minutes after an intradermal test with 0.05 cc. of a mixed antigen containing egg albumin (0.1 mg. nitrogen per 1 cubic centimeter). Ferguson⁷ has recently reported the case of a boy of six who received 0.18 cc. of antitetanus serum while under an intravenous anesthetic. It was given intradermally and death was preceded by development of a large wheal at the site of the injection. Boughton⁸ gave 0.06 cc. of horse serum intravenously to an asthmatic patient, aged twenty-nine, who succumbed in forty-five minutes. Freedman⁹ in 1935 reported a personal experience in which he gave a test dose of 0.05 cc. of horse serum intracutaneously to an asthmatic boy of six who had received an injection of diphtheria toxin-antitoxin at school twenty days previously. The child died in eight minutes despite vigorous treatment with adrenalin and artificial respiration.

Although injection of the foreign proteid in most of the fatal cases has been by the subcuticular or the intravenous route, my experience, Freedman's and Ferguson's cases and some of those collected by Lamson⁶ show definitely that the intradermal route may be just as dangerous to the hypersensitive person. For this reason, conjunctival or scratch tests are preferred. If the intradermal method is necessary, maximum precautions should be observed. The problem of treatment by serum of a hypersensitive person belongs to the skilled specialist in immunology quite as truly as resection of the stomach belongs to the skilled surgeon.

In this connection a comment by Rackemann¹⁰ bears repeating: "It is certainly true that where the degree of sensitiveness is exquisite, minute amounts of foreign serum are all that are required to produce a fatal reaction. The possibility of producing them in one case justifies the greatest caution in treating a hundred others."

To the clinician who is faced with the need to administer serum and wishes to do so with maximum safety, the recent paper by Rackemann¹¹ and the dicta laid down by Fantus and Feinberg¹² in 1936 are recommended. Several excellent textbooks¹³⁻¹⁵ are also available.

Inasmuch as transfusions are becoming increasingly common and blood banks are springing up all over the country, it seems advisable in the present state of our knowledge to exclude as blood donors the atopic allergic persons, especially those who are sensitive to horses. This advice is based on the classic experience of Ramirez¹⁶ of the unintentional passive transfer of horse asthma to a patient by a transfusion from an asthmatic person.

What has been said of precautions in relation to hereditary hypersensitive persons applies with almost equal force to that not inconsiderable portion of the population who may have been artificially sensitized by previous administration of serums, although the liabilities in this group are less grave.

SUMMARY

A recent case of sudden death from an intradermal injection of a minute amount of guinea-pig hemoglobin is reported. This case is correlated with that of the first case in this country of death from diphtheria antitoxin, and the familial hypersensitiveness affecting both is revealed.

The autopsy findings in both cases are stated, and attention is again called to the value of the Prausnitz-Küstner test as a post-mortem procedure.

Persons hypersensitive to the proteids of small animals are put in the same category as those who are sensitive to horses so far as the dangers of foreign-proteid therapy are concerned. Use of the intradermal route for preliminary testing is discouraged.

Meticulous observance of appropriate precautions in parenteral therapy by antigenic substances is urged.

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TECHNICAL CONSIDERATIONS IN EXCRETORY UROGRAPHY

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THIS study of 200 cases was undertaken to determine, if possible, the best preparation of patients for excretory urography. It is essential that one obtain clear films, unobscured by gas and fecal material, if plain scout films of the abdomen (kidney, ureter and bladder areas) and excretory urograms are to be of diagnostic value. If the blood urea is above 70 mg per 100 cc, it is unlikely that the kidneys will be able to excrete enough of the radiopaque medium in the concentration necessary to outline adequately the kidney pelves, ureters and bladder. Good visualization of the kidney pelvis in the film taken five minutes after the injection of the radiopaque medium generally denotes good function of that kidney, although the reverse is not always true.

Each of the 200 patients in this series received intravenously 20 cc. of Neo-Iopax (disodium N-methyl-3, 5 diodo-4 pyridoxyl 2, 6 dihydroxylate). No patient experienced vomiting, arm cramps or unpleasant symptoms, although a few complained of a feeling of warmth and slight nausea; these symptoms were readily alleviated by taking a few deep breaths. The absence of unpleasant symptoms can be attributed to four factors; the radiopaque medium employed, reassurance of the patient before the injection, the precaution of making certain that the 20 gauge short bevel needle was well within the lumen of the vein before the injection was begun and deep breathing by the patient immediately after the injection. Although it is generally recommended that the radiopaque medium be injected slowly, I found no correlation between the speed of the injection and the production of untoward symptoms. Furthermore, I have been unable to demonstrate the value of using an abdominal compression band or balloon in excretory urography, although in an occasional case a 5 to 10° Trendelenburg position may be of some value in obtaining a better filling of the kidney pelves.

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There was no uniformity of preparation in this series, since the patients were referred from various sources. This very lack of uniformity and the necessity of obtaining data concerning the preparation of each patient led to a study of the various resulting preparations and the time relation between the ingestion of food, the taking of water, castor oil and enemas and the making of the roentgenograms.

In each patient a plain scout film of the abdomen (kidney, ureter and bladder areas) was taken, the radiopaque medium was injected, and films were taken routinely five, twenty and forty five minutes after the injection. Each film was developed immediately. Delayed, upright and oblique films were taken as indicated by a careful observation of the wet films.

In patients with hypertension a three-minute film is imperative after the injection, because observation has revealed that the kidneys excrete the radiopaque medium very rapidly in the majority of these cases, so rapidly, in fact, that all the radiopaque medium, for reasons unknown, may be in the bladder within five minutes after the injection.

The excretory cystograms obtained should be studied carefully, for valuable diagnostic information may be revealed in regard to prostatic hypertrophy, diverticulums, nonradiopaque stones, extravesical pressure, tuberculosis "splinting" and tumors. An estimate of the residual urine, as well as information regarding the emptying of a diverticulum, if present, may be obtained by taking another film of the bladder area after the patient has voided.

In accident cases suspected of having a ruptured kidney, ureter or bladder, excretory urograms should be taken within two hours, if possible, because the intestines of these patients rapidly become distended with gas, which may interfere with adequate visualization of the lesion.

In this particular series, I avoided the use of Pitressin because of the unpleasant symptoms that

not infrequently result from its use. In carefully selected cases, its use is recommended.

The correlation between methods of preparation of the patient and the resulting plain scout films of the abdomen and excretory urograms is shown in Table 1. The films were graded as

TABLE 1. *Results of Preparation for Excretory Urography.**

GROUP No	No OF CASES	TYPE OF PREPARATION	RESULTS	
			PERCENT-AGE OF SATISFACTORY PREPARATIONS	PERCENT-AGE OF UNSATISFACTORY PREPARATIONS
1	23	No preparation	52	48
2	22	Castor oil at 7 p m , no enema	95	5
3	75	Castor oil at 7 p m , enema at 7 a m	53†	47
4	37	No castor oil, enema at noon	59	41
5	5	Castor oil at 7 a m , no enema	80	20
6	38	Castor oil at 7 a m ; enema at noon	89	11

*All the scout films and urograms were taken in the afternoon except in Group 2, in which they were taken in the morning

†Seventy seven per cent of scout films taken in the morning were satisfactory

satisfactory or unsatisfactory from the point of view of radiographic clearness and detail.

A study of the table reveals that the smallest number of satisfactory plain scout films of the abdomen and excretory urograms were obtained in patients who had no preparation (Group 1), who had 30 cc. of castor oil at 7 p.m. and a soapsuds enema at 7 a.m. (Group 3) and who had only an enema (Group 4). Plain scout films of the abdomen were made in the morning on all 75 patients in Group 3, and these were repeated in the afternoon immediately prior to the taking of the excretory urograms. Whereas 77 per cent of scout films of the abdomen taken in the morning were satisfactory, by afternoon only 53 per cent of the scout films and urograms were satisfactory, because the intestines in the interim had ballooned out with flatus, apparently owing to atony following the prolonged spasm produced by the castor oil.

Practically all the unsatisfactory scout films and excretory urograms were the result of flatus in the intestines. Enemas alone increased flatus, although if 30 cc. of castor oil had been taken the enemas caused less flatus because the castor oil apparently aided in expelling the air and water introduced with the enema. Another factor to be considered is that enemas may also interfere with the desired dehydration of the patient before excretory urography. Bed patients are difficult subjects to prepare satisfactorily for plain scout films of the abdomen and excretory urograms because of intestinal flatus, for rest in bed is not conducive to good gastrointestinal tone.

In groups receiving the same preparation in regard to castor oil and enemas, the best plain scout films of the abdomen and excretory urograms were obtained in the patients whose fluid intakes had been restricted to 250 cc. for the previous eight hours and who had not had a meal prior to the taking of the roentgenograms, while the poorest results were obtained in the patients who had eaten nothing for twenty-four hours. For reasons of brevity, the data substantiating these conclusions have been omitted.

Reference to the table shows that, other things being equal, the best results followed the oral use of castor oil alone (Groups 2 and 5), or castor oil followed in five to twelve hours by a soapsuds enema, provided that the roentgenograms were taken not later than fourteen hours after the administration of castor oil (Group 3—morning films—and Group 6).

SUMMARY

Factors conducive to the obtaining of satisfactory plain scout films of the abdomen and excretory urograms are evaluated in 200 cases.

It is concluded that castor oil alone and castor oil followed by a soapsuds enema in five to twelve hours, provided the films are taken within twelve hours after the administration of the castor oil, produce the most satisfactory results. Furthermore, fluids should be restricted for eight hours prior to taking the films, and an immediately preceding meal should be avoided.

MEDICAL PROGRESS

PROPHYLAXIS IN RHEUMATIC FEVER*

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BOSTON

A SPECIFIC agent for the prevention of rheumatic fever will probably not be available before the cause of the disease is known. Until that time, efforts directed toward prophylaxis must consist of general measures that have emerged from gradually accumulated knowledge concerning certain underlying and precipitating factors in the disease. It is obviously desirable to prevent the initial attack of rheumatic infection but, for practical purposes, efforts must be directed mainly toward the prevention of recurrences in patients known to be susceptible to rheumatic infection by virtue of previous attacks. If it were possible to separate the susceptible from the nonsusceptible by some simple test, such as the Dick or Schick test, the prevention of initial attacks might become possible.

The most widely held and best-supported view of the pathogenesis of rheumatic fever at the present time is that certain persons, because of hereditary or environmental factors, or both, have developed abnormal tissue reactions to hemolytic streptococci. The prevention of rheumatic attacks, therefore, is based largely on the prevention of hemolytic streptococcus throat infections.

Maintenance of proper nutrition and avoidance of fatigue and chilling are primarily aimed at increasing the patient's general resistance to infection. Of first importance is education of the patient and his family concerning the role of respiratory infections in rheumatic attacks and the strict necessity for protecting rheumatic subjects against such infections so far as possible. There is much to be said, from this point of view, in favor of special school classes for rheumatic children, where there is careful supervision, those in charge understand the problems involved, and the children are segregated from the general school population. In many parts of the country, rheumatic fever is a more pressing public-health problem than such diseases as tuberculosis and typhoid fever, yet no measures have been devised or undertaken to control the spread of what appears to be

a highly important precipitating agent in rheumatic fever—hemolytic streptococcus infection.

Hubbard and Griffin¹ instituted open-air sanatorium care for rheumatic children with the view of diminishing exposure to hemolytic streptococci. Bacterial counts of the air in the pavilions revealed few pathogenic organisms. At the beginning of the study 20 children with recent, but clinically inactive, rheumatic fever were admitted. There were no new admissions during the year. Visitors wearing masks and free of respiratory infection were allowed in the wards only once a week. None of the 20 patients developed respiratory infections or rheumatic activity. After returning home in excellent health their resistance to rheumatic fever appeared to continue. In addition to supplying confirmatory evidence of the relation between respiratory infection and rheumatic activity, the results also suggest that when the disease has become thoroughly quiescent, and not just subclinical, recurrences are less likely to occur. The prolonged treatment of an attack may thus become a safeguard against future exacerbations. It is to be hoped that further follow-up studies will be forthcoming.

HEREDITY

Wilson² has gathered evidence that susceptibility to rheumatic fever is transmitted as a single autosomal gene, and has compiled a table of prediction of the probable occurrence of rheumatic fever in the progeny. According to this table, if both parents have a positive history of rheumatic infection, nearly all progeny will become afflicted. If one parent is positive and a grandparent on the other side of the family is positive, the expected incidence in the progeny is about 50 per cent. If both parents are negative but one grandparent of each line is positive, the expected incidence is about 25 per cent. Although this knowledge is not likely to provide a fruitful field for the prevention of rheumatic infection, it should be kept in view in advising patients on the subject of marriage and childbearing. In any event, the offspring of families in which rheumatic fever is prevalent should be under close observation in order to detect the disease at its onset.

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CLIMATE

At one time streptococcal infections and rheumatic fever were thought to occur rarely in tropical and subtropical climates. In recent years this has been repeatedly refuted.³⁻⁶ There is, however, evidence that rheumatic fever is much less frequent and usually milder in the southern United States than in the northern temperate zone. Nichol⁷ found that rheumatic heart disease was only one third as frequent in native-born children in southern Florida as in children born in the northern states but residing in the South. Bailey⁸ believes that the disease is definitely milder in the South. He found that of a group of 42 children with illness ascribed to rheumatic infection, only 30 per cent developed signs of valvular damage, and in most of these the signs were minimal. Paul and Dixon⁹ studied the incidence of rheumatic heart disease in Indian children, and found that in the northwestern states 4.5 per cent of the children had signs of rheumatic heart disease, whereas in the southwestern states the incidence was only 0.5 per cent. The authors considered that all Indians are essentially similar in racial background, social and economic status and habits of hygiene, so that this striking difference must be attributable to the more equable climate in the Southwest. Several years ago Coburn¹⁰ transported 10 children with stubborn rheumatic infection from New York to Puerto Rico. The infection quickly became quiescent and remained so while the children resided in the tropics, but reappeared as soon as they returned to New York. Nichol⁷ was also impressed with the rapid subsidence of rheumatic infection in children transported from the northern states to southern Florida. Jones et al.¹¹ were less enthusiastic concerning their experience with transporting 26 rheumatic children from Boston to a subtropical climate. Whereas some of their patients did well, others continued to have active infection. Three died while in the South, and 2 others showed increased activity of the infection.

It is clear that transportation to southern climates is not the answer to the problem of rheumatic infection, not only because the disease may recur or remain active in such climates, but also because the economic status of the majority of rheumatic patients prohibits such migration. When permanent residence in tropical or subtropical climates can be arranged without hardship or financial sacrifice, it appears to be a reasonable prophylactic undertaking. However, there is the danger that such a move will produce a false sense of security and neglect of other more effective prophylactic measures. The evidence at hand indicates that it is better for the patient to

remain in the North and receive sulfonamide prophylaxis (see below) than to move to the South and receive no chemoprophylaxis.

TONSILLECTOMY

The relation between tonsillitis or pharyngitis and rheumatic infection has been noted for years. It seemed only reasonable to suppose that tonsillectomy might reduce the incidence of throat infections and, hence, rheumatic manifestations. Early statistical studies seemed to support such a thesis but, as emphasized by Wilson, Lingg and Croxford,¹² the age at operation, the period of observation and the inclusion of suitable controls are factors of importance sometimes neglected in such studies. These authors found that the incidence of initial attacks or recurrences was not significantly different in tonsillectomized or nontonsillectomized children. Recurrences were frequent in both groups under the age of nine years and less common in older children, irrespective of the presence or absence of the tonsils. Subsequent careful surveys¹³⁻¹⁷ have, on the whole, confirmed the absence of any striking beneficial effect of removal of the tonsils on the course of rheumatic fever.

In 1936, Kaiser¹⁸ reported the results of statistical analysis of a large group of children, which indicated that tonsillectomized children are somewhat less likely to develop rheumatic fever than nonoperated children and that the disease is severer in nontonsillectomized patients. He found the mortality rate to be nearly twice as high in children whose tonsils were present at the time of the initial attack. He concluded that statistical and clinical data justify the removal of tonsils in practically every rheumatic child, even though his figures did not indicate that the incidence of recurrences was favorably influenced by tonsillectomy. Furthermore, the difference in mortality rates was apparently dependent on removal of the tonsils in anticipation of the initial rheumatic attack. In 1940, Kaiser¹⁹ reaffirmed his opinion that fatal carditis is noted less frequently in tonsillectomized than in nontonsillectomized children.

The problem is an extraordinarily difficult one, not only because of the many variable, and often hidden, factors that affect the course of rheumatic fever, but also because of the more obvious, and neglected, factors of incomplete removal of the tonsils and of hypertrophy of the pharyngeal lymphoid tissue that commonly follows removal and that may serve as a focus of infection as effectively as do the tonsils themselves. The bulk of evidence at present is certainly opposed to the routine removal of tonsils because of rheumatic

susceptibility. All students of the problem are agreed that tonsillectomy should be performed in rheumatic patients when local conditions exist that are thought to indicate removal of the tonsils in nonrheumatic patients. There is also general agreement that the operation should be performed only after the infection has become quiescent, since otherwise an acute exacerbation may result.

VITAMIN C

One of the predisposing factors in rheumatic infection has appeared to be undernutrition, and of the various essential foodstuffs, vitamin C has attracted the widest attention. Rinehart²⁰ studied the pathologic lesions produced in guinea pigs maintained on an inadequate intake of vitamin C and infected with virulent bacteria. Lesions were thus produced in heart muscle, valves and joints, and subcutaneous nodules were formed that were similar to the lesions found in rheumatic fever. Most of the experiments were done with the hemolytic streptococcus, but this organism had no specific effect, since identical lesions were produced by other types of bacteria. In the presence of adequate vitamin C intake, infection with the same organisms did not produce the "rheumatic" lesions. In a subsequent study of plasma ascorbic acid levels, Rinehart, Greenberg, Olney and Choy²¹ found that in both active and inactive rheumatic fever there was usually an abnormal level and that, on the average, the level was lower than in a group of patients with miscellaneous infections. They postulated that the deficiency might be brought about by inadequate intake (namely, poverty), depletion by the disease or inherent metabolic fault.

Soon after the appearance of the reports on the experimental results in guinea pigs appeared, many investigators²²⁻²⁶ were led to try the effects of large doses of ascorbic acid on patients with rheumatic fever. The results were universally discouraging from both the prophylactic and the therapeutic point of view. Meanwhile McBroom, Sunderland, Mote and Jones²⁷ repeated the guinea-pig experiments and found that acute scurvy alone produced the same lesions that had previously been ascribed to chronic vitamin C deficiency and infection. The authors suggested that the diet used in the experiments of Rinehart permitted only moderate deficiency, and that the superimposed infection simply made the deficiency complete.

All observers are agreed that it is desirable to maintain adequate intake of all essential foodstuffs, but there are no data indicating conclusively that large amounts of vitamin C or any other food substance have any specific beneficial

action in the prophylaxis or treatment of rheumatic infection.

SULFONAMIDE PROPHYLAXIS

It has long been known that tonsillitis or pharyngitis frequently precedes an attack of rheumatic fever, and bacteriologic study of the offending organism has implicated Group A hemolytic streptococci. It has also been demonstrated by immunologic methods (antistreptolysin, antifibrinolysin, precipitin and agglutinin reactions) that most patients with rheumatic fever are suffering from either active or recent hemolytic streptococcus infections. It was only natural to hope that the sulfonamides, known to be effective against the streptococcus, might prove to be useful in the treatment of rheumatic fever. Unfortunately this was a false hope, for not only was sulfanilamide ineffective in the treatment of the disease, but patients were often made worse by the drug.^{28, 29} Toxic reactions with high fever were commonly seen, and congestive heart failure was not infrequently precipitated. Whether this latter effect was due to the toxic reaction, to the intensification of the rheumatic state or to a myocarditis produced by the sulfonamides³⁰ is not clear, but it soon became apparent that the drug was ineffective in combating the rheumatic infection, and that it was equally ineffective in preventing rheumatic manifestations if administered at the time of pharyngitis or tonsillitis due to the hemolytic streptococcus.^{28, 29, 31, 32}

The possibility of preventing hemolytic streptococcus throat infections by the administration of small doses of sulfanilamide over long periods of time to patients susceptible to rheumatic infection was then investigated, and reports by Coburn and Moore³² and by Thomas and France³³ appeared in 1939. Coburn and Moore³² administered sulfanilamide in doses of 2 gm. a day to 80 rheumatic patients during the winter and spring seasons, and only 1 of these developed hemolytic streptococcus infection and signs of rheumatic activity. The results of Thomas and France were equally encouraging, despite the use of smaller doses of sulfanilamide (1.0 to 1.3 gm. a day). They reported their results on 30 patients treated for two winter and spring seasons and included 30 control patients of approximately the same ages. In the treated group there were no major rheumatic episodes, whereas in the control group five such episodes occurred. Two minor attacks took place in both groups and, in addition, there were three questionable attacks of rheumatic fever in the control group. Important toxic reactions were not encountered by either group of investigators. In 1940, Coburn and Moore³⁴ reported on

a group of 184 subjects treated prophylactically with sulfanilamide, with an incidence of rheumatic attacks of less than 1 per cent, instead of the usual rate of 35 per cent.

Thomas, France and Reichsman³⁵ used sulfanilamide prophylactically in 55 patients. There were no serious toxic reactions and no patient developed a major attack of rheumatic fever. In a control group of 67 patients there were fifteen major attacks of rheumatic infection. The choice of control patients in earlier studies had been criticized on the ground that many of them had been placed in the control group because of indifference to the disease and an unwillingness to make the frequent visits necessary to the study. Such patients obviously might be expected to do less well irrespective of the use of sulfanilamide. Actually, Thomas, France and Reichsman found that the number of attacks was somewhat less in the unco-operative control group than in those patients who were placed in the control group for reasons other than unco-operativeness.

Coburn and Moore³⁶ presented a follow-up report on patients who had previously received sulfanilamide prophylactically. It occurred to them that the previously reported favorable results might have been due, at least in part, to the increasing age of their patients, with consequent diminution in susceptibility to recurrences. During 1939-1940, therefore, 100 patients who had received prophylactic treatment with sulfanilamide from 1936 to 1939 were taken off the drug. In this group 32 developed hemolytic streptococcus pharyngitis, and of these 40 per cent developed a recurrence of rheumatic fever. This follow-up study demonstrated that the rheumatic children who escaped while receiving sulfanilamide were still susceptible, when untreated, to streptococcal infection and rheumatic fever.

Stowell and Button³⁷ observed toxic effects of sulfanilamide in 19 of 46 patients treated prophylactically. In 25 per cent the drug was stopped permanently on account of rash, fever, nausea or lowering of the leukocyte count. One child died of agranulocytosis after twenty-nine days of sulfanilamide prophylaxis. The dosage was of the same order as that used by other investigators, that is, from 1.5 to 2.0 gm. a day in divided doses. The authors felt obliged to give up the prophylactic use of sulfanilamide because of the high incidence of toxic reactions, although they too reported fewer rheumatic recurrences in those who were able to tolerate the drug. Stowell and Button's report seems unduly pessimistic toward this form of therapy in the light of the accumulated experience of other investigators. Thomas³⁸ collected a series of rheumatic persons treated for 648 patient-

seasons, made up of her own cases and those of others, reported and unreported. The death reported by Stowell and Button was the only serious toxic reaction in this large series, whereas the prophylactic effects were excellent. There were only six rheumatic recurrences in the entire group—less than 1 per cent instead of the expected rate of approximately 30 per cent. Since then, Hansen, Platon and Dwan³⁹ have reported an additional 78 patient-seasons with only one recurrence (actually two recurrences, but one of these occurred six days after the beginning of sulfonamide therapy and should not be classed as a prophylactic failure). Toxic manifestations were seldom encountered, although in 1 case sulfonamide was discontinued when the leukocyte count dropped to 1700.*

There can be no doubt that prophylaxis of rheumatic fever with the sulfonamides is an important advance in the control of rheumatic fever. If patients receiving the drug are followed carefully, the incidence of toxic reactions of serious degree will certainly be far less than the mortality and morbidity of active rheumatic infection. Although the initial studies included a large variety of laboratory tests, experience has shown that, for practical purposes, prophylaxis may safely be carried on with frequent determinations of the hemoglobin level and the leukocyte count and an occasional test to the sulfonamide blood level. A number of observers have noted a gradual lowering of the leukocyte count during the first weeks of treatment with sulfanilamide, sometimes to levels as low as 2500, with a subsequent increase to normal without discontinuance of the drug. At such times the granulocytes may fall to 25 or 30 per cent.³⁸ In the event that such a fall does occur, daily leukocyte counts should be made and the drug discontinued if the count falls below 2000.

According to Thomas,³⁸ the drug should be begun before discharge of a patient following an attack of rheumatic fever because of the danger of exposure to respiratory infections in the home. The temperature and leukocyte count should be normal after withdrawal of salicylate, but there is no need to wait for the erythrocyte sedimentation rate to return to normal. Thomas further advocates that prophylaxis be continued throughout the year rather than for the winter and spring seasons only, since not a few recurrences come in the summer and fall, and that prophylactic sulfonamide be administered for five years or longer after an attack of rheumatic fever.

*Since this manuscript was prepared, Kuttner and Reysersbich⁴⁰ have reported on sulfanilamide prophylaxis in 108 patient-seasons with only one rheumatic recurrence. This brings the total reported patient-seasons to 834 with only eight rheumatic episodes instead of the expected rate of approximately three hundred rheumatic attacks. These authors report toxic manifestations in about 15 per cent of subjects receiving sulfanilamide.

Up to the present, sulfanilamide has been the chemoprophylactic agent reported on. In many clinics some of the less toxic sulfonamides, especially sulfadiazine, are now being evaluated. There is little reason to doubt that toxic reactions will be less troublesome, and no reason for supposing that sulfadiazine will prove to be less effective than sulfanilamide. In a small group of children treated prophylactically with sulfadiazine at the Massachusetts Memorial Hospitals for the past two years, the drug has been discontinued in only 1 case because of toxic reaction (rash and fever), and there has been no lowering of the leukocyte count during the early weeks of chemoprophylaxis such as has been observed with sulfanilamide. The number of subjects treated is too small to allow comparison of the effectiveness of sulfadiazine and sulfanilamide, but our experience suggests that sulfadiazine will prove to be more effective than sulfanilamide only in so far as a better tolerated drug will benefit more patients.

SALICYLATE PROPHYLAXIS

Following the demonstration by Derick, Hitchcock and Swift⁴¹ that aspirin (or neocinchophen) usually prevented the arthritis of serum sickness and that, in patients so treated, the production of precipitins against horse serum was inhibited, several investigators were led to try the effects of aspirin in the prevention of rheumatic fever. Leech⁴² treated 65 children with inactive rheumatic heart disease or potential heart disease with 20 gr. of aspirin daily for six months. Seventy-nine children served as controls. Definite rheumatic recurrences occurred in 7 per cent of the treated group and in 11 per cent of the control group. This is hardly a significant difference but, in addition, the author reported that the children who received aspirin enjoyed better general health, gained more weight and had fewer minor complaints than those who did not. Sheldon⁴³ was not convinced that a course of aspirin begun at the time of onset of pharyngitis was definitely beneficial, but admitted that it deserved further trial. Perry⁴³ administered aspirin in 10-gr. doses three times a day for twelve months to 41 rheumatic children. Recurrences occurred in 12 per cent of the treated group and in 18 per cent of a control group. Perry considered the difference insignificant, and attributed the better general health of the treated children to the fact that the parents of children receiving continuous medication of any kind are likely to be more attentive to details than the parents of children receiving no medication. Schlesinger⁴⁴ gave 7 to 12 gr. of aspirin three times a day at the onset of pharyngitis in rheumatic children. He reported

fewer rheumatic recurrences in children so treated and a much milder illness in those in whom recurrences did occur.

Coburn and Moore⁴⁵ administered sodium salicylate in doses of 60 to 90 gr. daily for one month to rheumatic subjects who developed pharyngitis and in whom Group A hemolytic streptococci were cultured from the throat. No patient with pharyngitis without this group of organisms received salicylates and none developed rheumatic fever. Forty-seven quiescent rheumatic subjects were given salicylates at the onset of hemolytic streptococcus pharyngitis, of whom only 1 developed rheumatic fever. Fifteen other patients showed a brief asymptomatic rise in the erythrocyte sedimentation rate after the withdrawal of salicylates. As a control group, 139 untreated rheumatic subjects with Group A hemolytic streptococcus pharyngitis were observed; of these, 57 developed recurrences of rheumatic fever. Coburn and Moore do not describe the nature or severity of the recurrences that appeared in the control group, and if one considers the 15 treated patients with elevated sedimentation rates as having mild, partially masked recurrences, the incidence of attacks was equal in both groups. It is probably safe, however, to assume that the difference in the two groups was impressive and significant, for these authors are well aware of the vagaries of rheumatic fever. It is of some interest that the titer of antistreptolysin was unaffected by salicylates, being essentially the same in both series of patients.

VACCINE PROPHYLAXIS

Small⁴⁶ isolated a nonhemolytic streptococcus from the blood and throats of patients suffering from rheumatic fever that he considered to be the etiologic agent and with which he prepared a vaccine and an antiserum. He reported that both appeared to be of benefit in the treatment of patients with rheumatic fever. Swift, Hitchcock, Derick and McEwen⁴⁷ isolated a streptococcus labeled "Strain Q33" from the tonsillar exudate of a patient with severe rheumatic fever and prepared a vaccine. In accordance with the view that rheumatic fever represents a hypersensitive reaction to streptococci and that animal experiments indicate that subcutaneous injection of antigen tends to sensitize, whereas intravenous injection diminishes tissue reactivity, the authors administered this vaccine intravenously in gradually increasing doses. Although very cautious in their claims, they believed that the results were encouraging. At the same time, Wilson and Swift,^{48, 49} using the same vaccine, reported a decrease in the number of recurrences of rheumatic fever in vaccinated children. Of the vaccinated group 45 per

cent remained free of recurrences for sixteen to twenty-four months, but only 18 per cent of the control series remained free of rheumatic fever. Later, however, Wilson, Josephi and Lang⁵⁰ were able to show equally good results with small doses of typhoid vaccine, so that improvement was either fortuitous or due to a nonspecific stimulation of resistance. These authors were led to the conclusion that vaccination with the various antigens used did not influence the incidence of rheumatic recurrences.

Coburn and Pauli⁵¹ immunized 52 nonrheumatic members of a nursing class (an equal number of subjects in the same class served as controls) with streptococcus toxin (Strain NY 5), beginning with 500 S.T.D. (skin-test doses) and gradually increasing the dose to 80,000 S.T.D. Each subject received between 300,000 and 400,000 S.T.D. The authors found no evidence that the course of immunization increased resistance to streptococcal infections or rheumatic fever. Wasson in 1933 began experiments on the immunization of rheumatic subjects with a filtrate made from Strain NY5. In 1938, she⁵² reported apparently beneficial effects in 34 subjects immunized with gradually increasing doses of vaccine administered subcutaneously. In 1940, Wasson and Brown⁵³ reported an incidence of rheumatic attacks in 10 per cent of immunized subjects, whereas in the control group recurrences occurred in 44 per cent. Unfortunately, the patients in the treated series were on the average four years older than those in the control group, that is, 12.9 years for the treated and 9.0 years for the controls. This factor alone may well have accounted for some of the difference in the incidences of rheumatic attacks. Another group of immunized children reported in the same communication⁵³ showed a similar diminution in the number of rheumatic recurrences, but again the treated patients were on the average older than the controls.

Wasson and Brown further reported follow-up observations on subjects previously immunized and found an incidence of rheumatic attacks in 7 per cent of patients previously immunized, whereas the incidence in the control group was 33 per cent. The average age in the latter series was actually slightly higher for the control group, being 12.0 years for the patients and 12.6 years for the controls. The authors thought that this indicated benefit after the cessation of the immunization program, but admitted that the control group was made up of unco-operative patients and that indifference to the disease might well have affected their general health and care. Recently the same authors⁵⁴ reported another series of immunized rheumatic subjects. Of 43 patients treat-

ed during 1939 and 1940, only 7 per cent developed rheumatic attacks, whereas in a group of 45 control patients the incidence of attacks was 40 per cent. In this series the average age of the treated and the control group was the same. During 1940 and 1941 the incidence of rheumatic attacks was 11 per cent in the treated and 33 per cent in the control group. As in the previous reports, follow-up studies showed continued benefits after cessation of the immunizing course.

Wasson and Brown also reported on the results of a modified and shortened course of immunization. A tannic-acid-precipitated toxin of Strain NY 5 was given intradermally in four injections of 5000, 8000, 10,000 and 12,000 S.T.D. at three-week intervals, following which 10,000 S.T.D. was given every six months. Forty-two subjects were so immunized, and during a nine-month period of observation there were no rheumatic attacks, whereas in 33 controls the incidence of attacks was 33 per cent. The average age for the treated group was 10.9 years, as compared with 12.1 years for the controls. If these results are confirmed, the procedure of immunization will be about as effective as sulfonamide prophylaxis and, in addition, will have the advantages of economy, safety and convenience. More investigation on the subject should be done, but in view of the unfavorable experience of Coburn and Pauli,⁵¹ using a vaccine prepared from the same strain of streptococcus, it is doubtful that such hopes will be realized.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29161

PRESENTATION OF CASE

A thirty-year-old salesman was referred to the hospital by his company physician because of a mass in the region of the upper lobe of the right lung.

Five days prior to admission an abnormal mass was found in the upper right-lung field in a chest plate taken as part of a routine physical examination. The patient was not subjectively ill and had no complaints. There was no dyspnea, orthopnea, palpitation, pain, cough, hemoptysis, fever, chills, night sweats, asthenia, fatigability or weight loss.

One week before entry the patient had contracted an upper respiratory infection with an associated moderate watery nasal discharge and a nocturnal cough productive each morning of a small amount of yellowish sputum. This cleared completely after four days without sequelae. The family and past histories were noncontributory.

Physical examination revealed a well-developed and well-nourished man who appeared comfortable. Several small (3 to 4 mm.), soft, movable, epitrochlear lymph nodes were palpable on the right side. The pupils were equal and round and reacted to light and accommodation. There was slight narrowing of the isthmus of Krönig on the right and questionable dullness to percussion at the right apex anteriorly, where the breath sounds were louder than on the left. The heart and abdomen were normal. Six to eight pea-sized yellow, subcutaneous nodules were felt in the scrotal skin. Rectal examination was negative.

The blood pressure was 130 systolic, 80 diastolic. The temperature, pulse and respirations were normal.

The red-cell count was 4,200,000, with a hemoglobin of 15 gm., and the white-cell count 7300, with 71 per cent polymorphonuclear neutrophils. The urine was normal. A blood Hinton test was negative.

A chest roentgenogram revealed a sharply rounded area of increased density measuring 8 by 10 cm. and lying in the posterior aspect of the right chest and extending to the apex (Fig. 1).

Fluoroscopically the mass seemed to move with respirations but not with swallowing. The right fourth rib was deformed. The chest was otherwise not unusual. In x-ray films of the dorsal spine the mass seemed to lie in the posterior mediastinum. The posterior aspects of the third and fourth ribs on the right side were spread, and there was a suggestion of erosion of the lower aspect of the third and the upper aspect of the fourth rib. The upper dorsal vertebrae showed no definite evidence of pressure defect. The neural canals were not visible.

On the eighth hospital day a thoracotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. RALPH ADAMS:* Perhaps we had better see the x-ray films first.

DR. LAURENCE L. ROBBINS: This is an excellent demonstration of the smooth homogeneous mass, which is located in the right upper-lung field. From its position I should say that it arises from the posterior mediastinum, although in the lateral view the lower bulge of the tumor seems to be in the midportion of the chest. There is definite separation of the ribs and apparent erosion. However, I think the entire fourth rib is abnormal. Otherwise the chest appears normal.

DR. ADAMS: The differential diagnosis for a lesion at the thoracic inlet requires three processes of deductive reasoning, based on the available data. First, one considers the anatomic sites from which the disease might originate, they being in this case the lung, the pleura, the neck and the mediastinum. Second, one enumerates the possible diseases for each site of origin, in this instance including tuberculosis and tumor for the lung, empyema for the pleura, a substernal thyroid gland and thymoma for the neck, and an esophageal tumor, aneurysm, embryonic arrest and neurogenic tumor for the mediastinum. Third, one analyzes the likelihood of each possibility as substantiated or negated by subjective and objective evidence.

Tuberculosis or tumor of the lung is unlikely because there had been no cough, sputum, hemoptysis or pain, the mass was encapsulated and lay medial to the lung, and there were no x-ray shadows indicative of change within the lung parenchyma.

Any area of encapsulation within the thorax and outside the lung may represent empyema, but if of this size, preceding fever or malaise would have been a part of the history. Furthermore, empyema of sufficient size and duration to cause rib erosion cannot exist without accompanying periostitis visible by x-ray, and evidence of periostitis is not seen on these films.

*Surgeon Lathrop Clinic.

The possibility that a substernal or plunging goiter arose in the neck is excluded by the absence of a palpable neck mass and by the lack of deviation or compression of the trachea. The thyroid

trachea begins near the hyoid cartilage and extends downward in a smooth arc, and the deviation is maximal at the greatest diameter of the thyroid tumor. By virtue of these facts one can anticipate

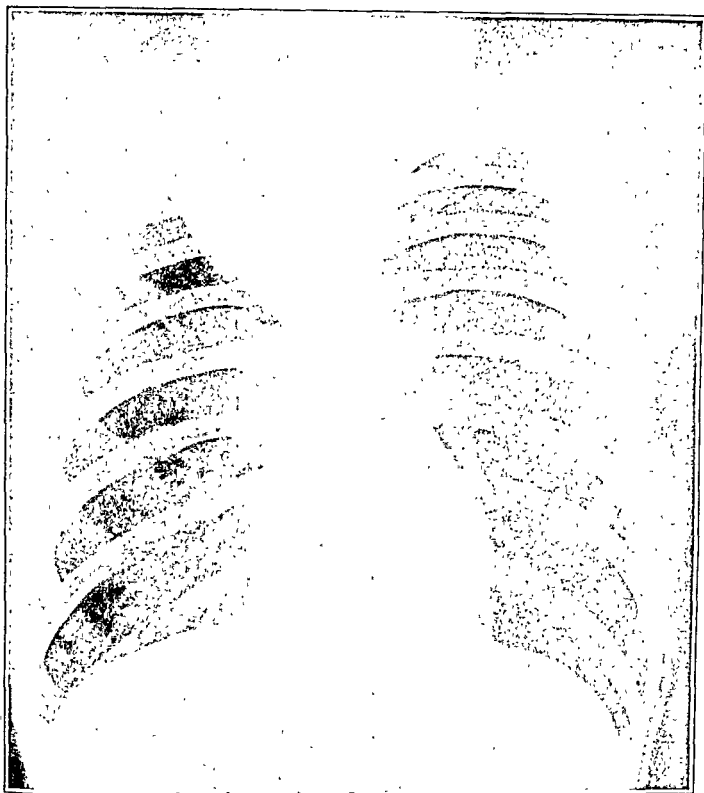


FIGURE 1. Roentgenogram Showing Mass in Right Upper Mediastinum.

gland is mentioned in the differential diagnosis of this case only because it must be considered whenever one is confronted with a unilateral upper mediastinal encapsulated mass. To gain access to the mediastinum, the thyroid gland must overcome the resistance of the first rib if it descends laterally, or the spine and manubrium if it descends anteriorly or posteriorly to the trachea. The disproportionate bony resistance always causes alteration of the tracheal contour, or at least there has been no exception to this statement in one large series of intrathoracic goiters. Two further facts may be of passing interest in relation to tracheal displacement caused by thyroid enlargement, as they are often of differential value. The curvature of the

the technical problems to be solved in the removal of a subclavicular or substernal goiter.

Since there were no symptoms of myasthenia gravis and since the left border of the mediastinum was not displaced laterally, the possibility of a thymic tumor seems too remote to merit discussion.

A tumor within the wall or lumen of the esophagus of such a size would certainly cause difficulty in swallowing and anterior displacement of the trachea, neither of which occurred.

Erosion and widening of ribs are among the classic signs of aneurysm, and this mediastinal mass has caused both. However, fluoroscopically visible pulsations within the mass and pain and

peripheral vascular abnormalities would be almost equally classic for an aneurysm in this location, but they are not recorded.

Cystic embryonic arrests, such as dermoid and bronchiogenic cysts, cannot by the fluid nature of their contents exert sufficient pressure to erode solid structures without themselves showing evidence of altered configuration. This mass showed no alteration of contour. A solid embryonic arrest, such as a teratoma, might cause pressure phenomena, but would usually be irregular in outline or exhibit some localized area of calcification. Most embryonic arrests are found in the anterior mediastinum, and that is contrary to the evidence in this case.

Tumors of neurogenic origin are not uncommon in the mediastinum. One type, von Recklinghausen's disease, may occur as a local example of a generalized disease. When so found, it represents an extension from the neural canal, and is accompanied by erosion of the vertebral articular facets. The diagnosis is untenable here because the facets were not eroded and there were no other stigmas of the disease.

A second type of neurogenic tumor characteristically arises asymptotically in the posterior mediastinum as a round dense mass, and by growth and pressure produces widening and erosion of the ribs in the costovertebral gutter. By reference to the record it is seen that a description of the typical features of this type of tumor is essentially a summary of the case under discussion. I shall therefore state my diagnosis as neurofibroma of the mediastinum.

DR. ROBBINS: I entirely agree with Dr. Adams's diagnosis but I think it is only fair to tell him something that is not given in the abstract, or for that matter in the original record. The resident who did the fluoroscopy thought that this mass changed in size with change in position. This was scoffed at because it did not show in the films.

DR. ADAMS: If it is true that the mass changed in configuration with change in position this indicates that it was not a solid lesion but a cystic one. That is a valuable bit of evidence. It would also indicate that the fluid was under enough pressure to erode solid structures. That is most unusual for a benign cyst such as a dermoid. I do not believe it could occur in a cyst of bronchiogenic or tracheal origin without displacement of the soft-tissue structures. A teratoma that started in a relatively benign fashion and then assumed malignant potentialities might have existed for a considerable time in the posterior mediastinum causing erosion in the way described and then might have grown rapidly with fluid in it.

CLINICAL DIAGNOSIS

Neurofibroma of mediastinum.

DR. ADAMS'S DIAGNOSIS

Neurofibroma of mediastinum.

ANATOMICAL DIAGNOSIS

Cyst of mediastinum.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The preoperative diagnosis on the wards was neurofibroma. I will read a portion of Dr. Robert K. Brown's operative note.

Approximately 25 cm. of the fifth rib was resected subperiosteally and the pleura opened. The lung was not adherent. In the upper portion of the right thorax lay an ovoid, pink, thin-walled cyst measuring 7 by 8 by 12 cm. No solid content could be felt in it. About half the cyst was retropleural, lying against the superior mediastinum, with the lower border in the angle between the azygos vein and the superior vena cava. The cyst was removed by sharp dissection, several small vessels being tied in the process. It lay adherent to the superior vena cava as noted.

The cyst itself was, as the operative note indicates, very thin walled and partially translucent. The wall consisted of fibrous tissue with a lining of low cuboidal undifferentiated epithelial or possibly mesothelial cells. It lay external to the pleura but in contact with it, so it could have been a pleural cyst, although its actual position was in the mediastinum. Certainly it was not a dermoid or tracheal cyst. It had no connection with the trachea or bronchi.

DR. ADAMS: How does the X-ray Department explain the findings?

DR. ROBBINS: It is the only case we have had of cyst of the mediastinum that showed rib changes.

DR. ADAMS: One would not have the right, on the evidence, to make a diagnosis of simple cyst.

DR. ROBBINS: No.

DR. ADAMS: Or, I believe, any diagnosis other than neurofibroma, on the basis of experience.

DR. ROBBINS: The one thing that was important was the observation of the resident, which was never followed up.

DR. BENJAMIN CASTLEMAN: Could the rib changes have been due to anything else?

DR. ROBBINS: As I look at the film, it seems as if the whole rib is abnormal, but there is also something that suggests erosion of the rib above, however. It may be congenitally abnormal.

DR. WILLIAM B. BREED: You do not know the source of the cyst?

DR. MALLORY: I cannot say with certainty. We called it a mediastinal cyst—a simple cyst. That does not mean much.

CASE 29162

PRESENTATION OF CASE

A twenty-four-year-old single engineer entered the hospital because of general malaise, fever and headache.

Approximately three weeks prior to admission, while at work, the patient felt weak and dizzy and had to return home. Several hours later he suffered with general malaise, a slight heavy "headachy feeling" and a temperature elevation to 99.6°F. During the next four days he rested, usually in bed, but felt well enough to take a physical examination for the army. During this period he suffered from nasal catarrh, occasional headaches and "fullness in the ears." Two and a half weeks before admission he suddenly felt worse; the nasal catarrh and postnasal drip became worse and his temperature rose to 103.5°F. He had no cough, chest pain, muscle or joint pains or urinary symptoms. His physician found the white-cell count to be 8000, with 80 per cent polymorphonuclear neutrophils, made a diagnosis of "grippe" and treated him with sulfathiazole by mouth. Several days later the patient entered a community hospital, where he ran a spiking temperature that frequently reached 103°F. and then was usually associated with shaking chills. The white-cell count averaged 20,000, with 90 per cent polymorphonuclear neutrophils, and blood cultures were positive for a nonhemolytic *Staphylococcus aureus*. The patient was treated with an intravenous course of sulfadiazine without success, and a focus of infection was never demonstrated. Chest x-ray films were said to have shown bronchitis and mastoid plates were negative. Agglutination tests for typhus, typhoid and paratyphoid fevers were negative. A lumbar puncture done four days prior to admission to this hospital showed an initial pressure of 170 mm. of water; the dynamics, protein and sugar levels and cell count were not reported.

The family history was noncontributory. As a boy, an eardrum was lanced for otitis media without known sequelae. Recently the patient had been subject to frequent grippy colds. There was no history of rheumatic fever.

Physical examination disclosed a pale, thin, sick man who moved about slowly. The neck seemed stiff on forward flexion, but movements were not painful. Both eardrums were retracted, with slight reddening of the centers. The heart was

slightly enlarged to the left, the apical impulse being felt in the fifth intercostal space, where a soft systolic murmur was audible. The second pulmonic sound was sharp and reduplicated. The lungs and abdomen were normal. Slight tenderness was present over the spine at the level of the eighth dorsal vertebra. The neurologic examination was not abnormal.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 103°F., the pulse 110, and the respirations 30.

The hemoglobin was 12.2 gm., and the white-cell count 14,000. The urine was acid, had a specific gravity of 1.015 and showed a green sugar test (the patient had recently received a glucose-saline infusion); the sediment contained 1 white cell and an occasional epithelial cell per high-power field. The prothrombin time was 33 seconds (normal, 18 seconds). A blood Hinton test was negative. Blood cultures repeatedly contained a coagulase-positive, hemolytic *Staph. aureus*. The nonprotein nitrogen was 20 mg., and the protein 5.7 gm. per 100 cc., and the chloride was 96.0 milliequiv. per liter.

X-ray films of the sinuses showed no definite evidence of disease. Those of the spine showed slight haziness of the ninth vertebra, but a definite lesion was not demonstrated and the disk space appeared to be of normal width. A film of the chest revealed a hazy density in the left mid-lung field that appeared to be in the upper lobe. There was also haziness close to the septum at the base of the left lower lobe, and a small amount of fluid was present in the left pleural cavity. There was no shift of the mediastinum, and the right lung field was clear. The heart was not definitely abnormal although the left border was prominent. In the flat plate of the abdomen the kidney outlines appeared normal. There was an area of density overlying the right sacroiliac joint that might have been within the bone. No abnormal gas or soft-tissue shadows were visible.

A lumbar puncture revealed no initial pressure. When the head of the bed was raised the pressure rose to 110 mm. Good cardiac and respiratory oscillations were never obtained, but on straining for ten seconds, the pressure rapidly and steadily rose to 200 mm. but fell immediately to 110 mm. Compression of one jugular vein produced no rise, but bilateral compression occasionally produced a slow unsteady rise to 140 mm. After release there was a slow irregular fall to 110 mm. Then with the patient in a semisitting position, 10 cc. of clear, colorless spinal fluid was obtained; this reduced the pressure from 110 to 65 mm. The fluid contained 8 red cells, 2 large round

cells and 1 small round cell per cubic millimeter, and the total protein was 26 mg. per 100 cc.

The patient was treated with large doses of intravenous and intramuscular penicillin and adequate courses of orally administered sulfathiazole and sulfadiazine. However, he continued to run a spiking fever, became more ill and had shaking chills. The dorsal vertebral tenderness seemed to clear. The white-cell count ranged to 24,600. Occasionally a + test for albumin developed in the urine, and at such times the sediment contained a few red and white cells. An x-ray film of the chest on the forty-eighth hospital day disclosed mottled density in the base of the right upper lobe and new areas of density in the left lung, and there appeared to be small areas of rarefaction in the areas of density previously described. There was fluid in both pleural spaces and when this was aspirated from the left side it was found to be slightly blood tinged, but negative on culture.

Throughout his entire illness the patient suffered with frequent shaking chills and areas of consolidation developed in various parts of the lung fields. Examinations of the heart revealed only the apical systolic murmur heard on admission, though later a gallop rhythm developed. Repeated electrocardiographic recordings were within normal limits. Terminally, abscesses developed in the left lung and the sputum contained *Staph. aureus*. Albuminuria developed, and the urinary sediment contained red and white cells and sulfadiazine crystals. Four days prior to death he was treated with 25 gm. of sodium sulfadiazine administered in a 500-cc. saline infusion; this produced a blood level of 101 mg. per 100 cc. On the next day the urine showed a +++ test for albumin, occasional red and white cells and many sulfadiazine crystals. The non-protein nitrogen was 82 mg. per 100 cc., and the chloride 95 milliequiv. per liter.

Two days prior to death the patient became cyanotic, and later comatose. A tension pneumothorax on the right side was relieved by suction. Several hours before death, subcutaneous emphysema of the chest developed; dyspnea suddenly increased, and he rapidly failed, dying two months after admission.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM BECKMAN: The symptoms of malaise and fever, the spiking temperature and rapid pulse, and the high white-cell counts all indicate that this patient was suffering from sepsis. The numerous blood cultures that were positive for staphylococcus make it fairly evident that the sepsis was due to this bacterium. That is further confirmed by the fact that the strain was coagulase

positive, such staphylococci being more frequently pathogenic than the coagulase-negative ones. Of course staphylococci do not just develop in the blood stream: one must search for some source from which they might have been entering it. This site is not obvious from any of the data presented in the case record. However, the onset with a cold and definite ear involvement suggests that it must have been something that arose in the ear. The obvious thing to think of with middle-ear infection is mastoid involvement, but we have a clear statement from the x-ray examination that the mastoid processes were not involved, so this seems improbable.

The next thing one would think of is thrombosis of a lateral sinus. This could occur with minimal ear disease, the infection being transmitted from the ear to the sinus through small veins, with the formation of a septic thrombosis. The fact that he had a stiff neck is suggestive of this. I think that is what the patient had. At least it is the best I can do in discovering the primary focus on the basis of such information as we are given in the case.

Incidentally, the lumbar-puncture findings are perfectly satisfactory for the diagnosis of sinus thrombosis. The fact that jugular compression did not produce a rise in pressure is suggestive, though not diagnostic. Certainly cases of sinus thrombosis have been reported in which there was no more cellular response in the spinal fluid than there was in this case.

If we postulate that the patient had a sinus thrombosis, and if it was infected with staphylococcus, it is easy to understand the staphylococcal septicemia, and all the other features of the case can be explained on that basis. We have definite x-ray evidence of increasing infection in the lungs, which probably means that emboli were being sent from the infected thrombus to the lungs from time to time, thus producing more and more abscesses. This is a good time to look at the x-ray films.

DR. LAURENCE L. ROBBINS: Only the films that show the course of the lung changes as the disease progressed are presented. On the first examination there is comparatively little to be seen in the chest. There is a small amount of density in the left costophrenic angle, suggesting fluid there. There is this shadow in the left midlung field, which is consistent with infarct. There are also finely mottled areas suggesting atelectasis in the right lung field but nothing about which one can be positive. Then as the disease progressed we see that new areas of density appear, as well as a large area on the right side. About a month after he had been in here we were fairly sure that there were cavities in the areas of density and that the areas

represented septic infarcts. The terminal film shows that there is pneumothorax as well, but since it was taken with a portable machine, it is not too satisfactory.

DR. BECKMAN: Can you tell anything about the density of the ninth dorsal vertebra?

DR. ROBBINS: We were never sure that the density meant anything, and it never was followed further.

DR. BECKMAN: I do not see how it fits in with anything I know about this patient. Possibly I am missing an important clue.

In addition to the fact that we have this excellent roentgenological evidence of continuing metastatic infarction of the lungs, it appears to me there is similar evidence of metastatic disease of the kidney. We know there were organisms in the peripheral blood because they were grown in blood cultures, and logically one can surmise that they would go to the kidneys too. From time to time the patient showed small amounts of albumin in the urine associated with red and white cells, and I think it is proper to consider that these findings represent metastatic infection of the kidneys. In addition, however, he was receiving the sulfa drugs, which we know damage the kidney, and later on in the disease he showed drug crystals, which might have accounted for some of the red cells, white cells and albumin present at that time. When I first read that the patient was given 25 gm. of sodium sulfadiazine at one time, I thought it might be a misprint, but when I saw that he had a blood level of 101 mg. per 100 cc. I knew it would be impossible to have two such misprints in the same sentence; so I presume that that dose of sulfadiazine was administered. I know nothing about the indications for such enormous doses. I feel sure that here it was a heroic measure in a patient obviously dying. The reason we do not know more about this method of therapy is that few of us have the courage to try large doses. However, with such a high blood level and with many crystals in the urine it seems probable that some of the renal damage, particularly after this large dose, was due to sulfadiazine. The next day the serum nonprotein nitrogen had risen and there seems to have been a rapid change in the kidney situation at that time, which further suggests that the drug had injured the kidney.

Another organ that is apt to be involved in cases of septicemia is the heart. Usually it is involved in the form of acute endocarditis. So far as I know, there are no special signs or symptoms of acute endocarditis. There was very little change in the heart throughout the entire course of the illness that could not be accounted for by the fact that

the patient was going downhill, and I do not see how one can rule in or out acute bacterial endocarditis due to staphylococcus. But I shall say that he did have it, since it is highly probable that a staphylococcal septicemia for two months would result in such a lesion.

The final episode seems to have been a rupture of one of the lung abscesses into the pleural space, producing a pneumothorax with some sort of valve mechanism because the pneumothorax was under tension and had to be relieved by tapping the chest. I should also guess he had empyema if an abscess had ruptured into the cavity. I do not believe, however, that coma is a symptom of spontaneous pneumothorax; that probably has to be explained in another way, most likely by a terminal meningeal involvement by the staphylococcus.

So to sum up I shall say that the patient had a middle-ear infection that led to thrombosis of the lateral sinus, which in turn gave rise to staphylococcal septicemia with metastatic abscesses in the lungs, acute endocarditis, metastatic infection of the kidneys, terminal rupture of an abscess of the lung into the pleural space with empyema and, finally, invasion of the meninges.

DR. PAUL D. WHITE: If the lung involvement was due to septic infarction, the emboli would not have gone through the heart and lungs to the kidneys unless there was a paradoxical embolism by way of an auricular septal defect.

DR. BECKMAN: We know that there were organisms in the other side of the circulation because blood cultures from the arm vein were positive.

DR. CHAMP LYONS: May I add a note to that? I have been a long time trying to convince myself that it is true. We have had a patient without left-sided endocarditis who had petechiae of the skin and who, at autopsy, showed kidney abscesses of the infarct type. He had septic pulmonary lesions with secondary pulmonary venous thrombosis, which served as a source of septic emboli.

DR. TRACY B. MALLORY: It is a possible, but on the other hand not usual, source of widespread miliary emboli.

DR. LYONS: It is rare, but I have seen it.

DR. WHITE: I saw this patient several times because of the obscurity of the site of infection. I never found any proof of heart disease, but thought that there might have been right-sided endocarditis. Since the pulmonary valve never caused murmurs and since one does not expect to get murmurs when the tricuspid valve is involved, I postulated a tricuspid lesion.

DR. LYONS: I believe we committed ourselves to a diagnosis of right-sided endocarditis. So

far as our experience goes, such a persistently positive blood culture under penicillin therapy probably means endocarditis, and without other obvious foci we came to the diagnosis of right-sided endocarditis. I might add that, like other patients with staphylococcal bacteremia, this patient ran a persistently elevated prothrombin time, which we were able to control only with repeated blood transfusions. The massive sulfonamide dosage was a desperate effort undertaken at the request of the man's father, who was a physician.

CLINICAL DIAGNOSES

Vegetative endocarditis of tricuspid valve.
Staphylococcal bacteremia.
Multiple septic pulmonary infarcts.
Pyopneumothorax, right.

DR. BECKMAN'S DIAGNOSES

Otitis media, purulent.
Sinus thrombosis.
Bacterial endocarditis, acute (staphylococcus).
Septic infarction of lungs, with abscess formation.
Abscesses of kidney.
Pyopneumothorax.

ANATOMICAL DIAGNOSES

Endocarditis, tricuspid valve, acute (*Staphylococcus aureus*).
Infarcts of lungs, multiple, septic, with abscess formation.
Rupture of abscess, with pyopneumothorax.
Emphysema, subcutaneous, of chest wall.
Acute glomerulonephritis.
Sulfonamide crystals in urinary tract.

PATHOLOGICAL DISCUSSION

DR. MALLORY: I am not able to prove whether Dr. Beckman's primary diagnosis is right or wrong. We were not permitted to examine the head. We did find, however, endocarditis of the tricuspid valve, with a vegetation measuring 1 by

2 by 3 cm., which was so big that it projected into and partially filled the auricle. There were no vegetations on the other valves. The lung showed multiple septic infarcts in all stages of development, and one of them had ruptured into the pleura, causing pyopneumothorax.

The kidneys, of course, were of interest. We were able to find practically no evidence of sulfonamide damage except for the presence of crystals in the pelvis; there was nothing in the parenchyma that one could attribute to the drug. On the other hand, every glomerulus was swollen and contained more nuclei than it should, and I think we have to make the diagnosis of acute glomerulonephritis. We are accustomed to associate glomerulonephritis with streptococcal infection and it is certainly a rare concomitant of staphylococcal infection. Every glomerulus showed diffuse involvement, not the focal embolic involvement that one sees with bacterial endocarditis on the left side of the heart.

DR. WHITE: How often do you find evidence of previous rheumatic involvement of the valves in these cases?

DR. MALLORY: I think that in most cases the valves have seemed normal except for the acute endocarditis. There was no suggestion here that the tricuspid valve had been previously damaged.

I rather hurriedly looked up a number of old cases of primary bacterial tricuspid endocarditis which are not very numerous, and found that my impression that the pneumococcus was the most usual organism was apparently correct. Over half the cases were due to the pneumococcus; next came the staphylococcus, with the streptococcus running third.

DR. BECKMAN: You do not know what the defect was in the dorsal vertebra?

DR. MALLORY: We could find nothing.

DR. LYONS: It is only fair to add that we, on the wards, had the benefit of Dr. LeRoy A. Schall's opinion that sinus thrombosis could be ruled out with a fair degree of certainty.

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THE SOCIOECONOMIC BURDEN OF CRIPPLING DISEASES

The burden of the crippling diseases is growing heavier. The average duration of chronic diseases in persons over fifty years of age has more than doubled in twenty years. In 1870 seven persons were living in the productive years from twenty to sixty to one person in the nonproductive years after sixty. In 1930 there were only five and a half productives to one nonproductive, which represents a loss of 23 per cent in sixty years. As Bigelow and Lombard¹ stated, "There is hardly a family in Massachusetts without immediate experience with cancer, heart disease or rheumatism."

Excepting mental disease, the chronic and crippling diseases that are of chief concern to the sufferers themselves and to the taxpayers of any nation may be listed in the inverse order of their importance as follows: congenital defects and birth injuries, diseases of the locomotor and skeletal systems, tuberculosis, diabetes, nephritis and renal disorders, cancer, major cardiac and circulatory disorders, and chronic rheumatism. The findings of the careful and authoritative study of the incidence and the implications of chronic disease in Massachusetts were reported by Bigelow and Lombard¹ in 1933. They concluded "Rheumatism . . . cripples in the largest number and kills in the smallest. This very ability to cripple without killing would seem to put it in the lead of all other chronic diseases as of pre-eminent social, economic and medical importance." Moreover they found that, with the exception of chronic diseases of the eyes and ears, the chronic rheumatic diseases were receiving the smallest amount of medical attention—over 68 per cent of persons affected by these diseases either were receiving no medical treatment or were treating themselves.

At the present time the facilities for early diagnosis, research, discriminating therapy, hospitalization, and undergraduate and postgraduate medical education are sadly inadequate to cope with this "king of human misery," who crippled the human prototype, the Ape Man, two hundred million years ago. But, as Bigelow and Lombard¹ stated: "The pall of hopelessness among the 'profession' in regard to effective therapy is even more atrophy-ing than that of the public. . . . All resources, private, philanthropic and governmental, must be enlisted. Complacency is wicked and dangerous." These are strong words but they need more emphasis today than when they were written ten years ago.

An excellent editorial² on crippling diseases appeared in the January 30 issue of the *Lancet*. It defines crippling disease as a disorder that leads to incapacity, calling attention to the fact that the chronic rheumatic diseases probably lead to more

crippling, greater suffering and higher economic loss than do any other medical disorders. It has been estimated that more than a million patients in England annually consult physicians because of the chronic rheumatic diseases, which cause one sixth of the total invalidity of the insured population. The annual cost of these diseases in England and Wales is believed to be at least £20,000,000, and an equally serious state of affairs has been found to exist in Scotland. In 1935 it was estimated that in the United States, disability resulting from the chronic rheumatic diseases represented an annual wage loss of more than \$200,000,000, and it was said that in 1931 about 35,000 ex-service men received over \$10,000,000 in disability compensation for arthritis and that the figure was increasing yearly.³

The Empire Rheumatism Council, of which Lord Horder is chairman, the British Orthopaedic Association and the Scottish Orthopaedic Council have advocated the establishment of one or more special hospitals for the treatment of the crippling diseases in each medical region of Great Britain as a means of lightening the social and economic burden of these crippling diseases.

Several years ago Dr. Frederick A. Washburn, formerly director of the Massachusetts General Hospital and subsequently commissioner of the municipal hospitals of Boston, suggested as a result of his experience, and for what seem to be cogent reasons, that units for the investigation and treatment of the crippling diseases should be established and administered by a large general hospital of high standing that was affiliated with an important medical school. Under such a plan the cost of building and administration would be greatly reduced, diversified laboratories would provide opportunity for research, consultants in medicine, surgery and the specialties would be available daily, the training school would solve the nursing problem and undergraduate and postgraduate education would be made easy. The conviction is growing that Dr. Washburn's plan is sound. In such units the chances of finding the solutions of some of the vexing problems that the crippling

diseases present would be much better than they would be in the special hospitals proposed by the *Lancet*. Today, solutions are paramount and should be the order of the day.

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AMERICAN MENTALITY RE-ESTABLISHED

AS UNREPENTANT, even if untutored, practitioners of the basic art of psychology, we physicians of the family front should show a particular interest in the issue of *Fortune* for December, 1942. In this number our opulent contemporary goes all out on a crusade to end once and for all the unhappy determination of the majority members of the American public to classify the other adult millions as possessing the average intelligence of thirteen-year-old children. Such a belief, now branded by *Fortune* as an outrageous libel, dates back to World War I, when large groups of American troops scored an average mental age of thirteen years in the Binet intelligence test. Since that time the average American, although convinced that he himself knows his way around,—and how,—has pityingly accepted for his colleagues in the art of living the intellectual status that had been so enthusiastically established for them.

This myth has, of course, its value, for in each of us a decided sense of well-being results from the consciousness of our superiority to the impotent proletarian ground swell that continually breaks against the solid foundations of our ego; it is another matter when the press, the radio, Hollywood, the advertising fraternity and even our representative, if somewhat zealous, government adopt the same attitude.

That attitude on the part of all these agencies probably had its uses when the road was relatively smooth and each gas tank was full to overflowing. It showed, in fact, a smartness not usually attrib-

uted to the thirteen-year-old mentality—we were willing to let someone else do the worrying when there was little or nothing to worry about. Childish behavior, too, in moments of relaxation, which has been taken to indicate a goon-like vacuity, is by no means the high sign of a childish mentality. Our national sense of humor is a powerful defense that our grimmest enemies have never yet been able to penetrate.

When reality does present itself, however, we prefer to be allowed to face it as such. As a nation and as individuals we have come of thinking age and have a right to expect a mature approach. We have a right to be told our bad news without sugar-coating—good or bad, it belongs to us. We have a right, rarely granted, to listen to radio programs without being harried by hypophrenic advertising plugs. We have a right to expect that our leaders, elected, appointed or self-selected, will treat us as fellow citizens and not as particularly helpless babes in the wood; that they will be leaders and not drivers, executive officers and not police officers.

We have a right not to be talked down to as children, but to have our problems and our obligations explained in clear and simple terms, free of legalistic indirection. We have a right to be told, by acknowledged experts, the state of our natural resources and our individual relations to them; we have a right, after we have cheerfully accepted the rationing of any commodity, to be allowed the free use of it, within that restriction, without being forced to accept the outrage of being spied on, bullied and police-ridden—this, happily, is at last coming to pass. We have, moreover, the right to ask for a clear and sensible definition of that bedeviling term “pleasure driving” or that its use be dropped for the duration!

MEDICAL EPONYM

TRENDELENBURG POSITION

This was described by Friedrich Trendelenburg (1844-1925) of the University of Bonn in an article entitled “Ueber Blasenscheidenfisteloperationen

und über Beckenhochlagerung bei Operationen in der Bauchhöhle [Operations for vesicovaginal fistula and elevation of the pelvis in abdominal operations],” which appeared in Volkmann’s *Sammlung klinischer Vorträge* No. 355 pages 3373-3392, Leipzig, 1890.

If the patient’s body is so placed on the operating table that the symphysis pubis is the highest point of the trunk, and the axis of the trunk forms an angle of at least 45° with the horizontal, then all the viscera, but especially the liver, spleen and mesentery, fall by their own weight into the hollow of the diaphragm. The intestine follows and falls out of the true pelvis, so far as air pressure permits. . . . If one now makes either a longitudinal or horizontal incision in the hypogastric region for the purpose of removing a stone, and splits the recti together with the underlying fascia, air will immediately enter into the prevesical space, often with an audible sound. The peritoneal fold drops down, and the narrow prevesical space becomes a gaping, well-lighted cavity in which the anterior wall of the bladder and the surrounding fold of peritoneum may be seen. . . . The value of elevation of the pelvis is equally striking in intraperitoneal operations in the pelvic cavity and the lower part of the abdomen.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

INTESTINAL OBSTRUCTION IN A NEWBORN INFANT

S. M. was the first child of a normal mother and father. Pregnancy had been uneventful and delivery occurred at full term after a short and easy labor. The birth weight was 5 pounds, 12 ounces. Twenty-four hours after delivery, when the child was put to the breast, she nursed normally but vomited shortly afterward. The vomitus contained mucus and milk curds. Slight cyanosis was noted, and although physical examination was normal, a roentgenogram of the chest showed partial atelectasis of the left upper lobe. The vomiting was considered of no significance, but the atelectasis caused some concern. However, on the second day of life the child’s color improved and a check roentgenogram showed the lungs to be well expanded. During the second and third days of life vomiting continued and became definitely projectile in nature. Apparently the vomitus did not contain bile. Gastric lavage had no beneficial effect. On the second and again on the third day a meconium stool was passed.

Physical examination at the age of three days showed an infant who was normal in appearance

except for slight dehydration. There was no generalized distention of the abdomen—in fact, the lower two thirds of the abdomen was quite flat. The epigastrium was somewhat full. Close inspection showed a few visible peristaltic waves, apparently gastric in type, passing from the left to the right side of the epigastrium. No abnormal masses could be felt within the abdomen. By auscultation the lungs appeared to be well aerated.

The red-cell count was 5,000,000, with a hemoglobin of 100 per cent, and the white-cell count 7600. Roentgenograms of the abdomen were taken with the child in a prone and also in an erect position. These showed considerable gaseous dilatation of the stomach, in addition to a large bubble of air that presumably represented a dilated first part of the duodenum. No gas could be seen in the abdomen below this level. The findings were suggestive of a duodenal obstruction, and it was deemed advisable to explore the child without further study by a gastrointestinal barium series.

Operation was undertaken under local novocain infiltration of the abdominal wall. The stomach was dilated, and the pylorus patulous. The first portion of the duodenum was enlarged to about three times its normal diameter. The pancreas extended far to the right, and its head surrounded the second portion of the duodenum—a so-called “annular pancreas.” This constricted and obstructed the duodenum. Only a few small bubbles of gas were present in the tiny, collapsed intestine beyond the second part of the duodenum. The lumen of the duodenum at the point of obstruction was not more than a millimeter or two in diameter. So far as could be seen, the extrahepatic biliary system was normal. To relieve the duodenal obstruction, an antecolic, isoperistaltic duodenojejunosomy was performed, using two layers of fine silk to effect the anastomosis. The baby stood the procedure well and was returned to bed in a satisfactory condition.

For the first two postoperative days all fluids and nourishment were given by parenteral routes. On the third day she was placed on two-hour feedings, beginning with water, changing to whey, and finally employing breast milk. After the fourth day a cow's milk, Karo and water formula was used, increasing the volume of the feedings and increasing the time interval between feedings, so that the baby was taking full caloric requirements on a four-hour schedule at the time of her discharge from the hospital on the eighth postoperative day. The abdominal wound healed per primam.

Following discharge the baby has taken feedings normally, has had a satisfactory gain in weight

and has progressed normally in every way during the six months that have elapsed since operation.

Comment. Intestinal obstruction in the newborn infant may be due to a variety of causes. In this case an unusual one was encountered, but whether the obstruction is due to such a rare anomaly or to some other cause, such as malrotation of the bowel, mesenteric band, congenital stenosis or atresia, imperforate anus or meconium ileus, the manifestations tend to be more or less similar, depending on the degree of obstruction and the level at which it occurs.

Because most of these conditions are amenable to skillful surgery an early diagnosis is of primary importance. This begins with a knowledge of the etiologic possibilities that may underlie what at first appear to be minor symptoms. With a suspicion of this sort, the physician should question the nurses regarding the mechanical aspects of feeding and then carefully observe the appearance of the abdomen. Because the neonatal intestine normally contains so much air, helpful assistance can be gained from a roentgenogram. The anatomic level of obstruction can be substantiated by films taken with the infant in various positions; if the air-filled portion of the bowel terminates sharply at the same level when the infant is photographed suspended head downward as when a film is made in the normal upright position, the probability and the site of an obstruction become more definitely established. Meconium may be passed quite normally in the presence of high obstructions such as this one, so that although its failure to appear is significant, its presence does not alter the diagnostic probabilities.

The refinements of pediatric surgery now offer a considerable chance of successful result in operations on newborn and even premature infants. Unsuccessful results may be traced to delays in diagnosis as often as to any other single cause.

WAR ACTIVITIES

INDUSTRIAL MEDICINE

TUBERCULOSIS IN INDUSTRY

Seventy-seven war industries in 11 states were surveyed by the eight 35-mm. photofluorographic units operating in industry prior to February 1, 1943, reports the Office of Tuberculosis Control, United States Public Health Service.

A total of 194,896 individuals were x-rayed. Tabulations on results are available for 125,190 people. Of these 1631, or 1.3 per cent, were found to have significant pulmonary tuberculosis. The distribution of the positive cases by stages of the disease was as follows: 874, or 53.6 per cent, minimal; 707, or 43.3 per cent, moderately advanced; and 50, or 3.1 per cent, far advanced.

In the District of Columbia 28,098 government workers have been x-rayed. Exactly 300 cases of pulmonary tuberculosis have been discovered, an incidence of 11 per cent. Of these 182 (60.7 per cent) were minimal, 106 (35.3 per cent) moderately advanced, and 12 (4.0 per cent) far advanced. In addition, 1300 workers at the National Institute of Health have been x-rayed. Among these, 15 cases of tuberculosis were found—9 minimal and 6 moderately advanced.—Reprinted from *Industrial Hygiene* (March, 1943), a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

MISCELLANY

FAR CHALLENGES THE GENERAL PRACTITIONER

Fire is fire, no matter what the fuel, but when gasoline is thrown on a flame a dangerous explosion results. Tuberculosis is the same disease now as in prewar time, but it invariably favors a flare-up of tuberculosis and creates new difficulties for those who must combat the blaze. The hard pressed general practitioner is a seasoned firefighter whose aid must be enlisted and whose effort must be supported if smoldering tuberculosis, lately coming under control, is to be prevented from spreading into serious conflagration. Even veteran firemen however periodically examine their equipment and drill themselves to increase their efficiency. A recent article by Perry, P. General Practitioner's Role *Bulletin of the National Tuberculosis Association*, March, 1943) emphasizes many of the important points and is abstracted below.

Under the stress of war it has been observed that conditions favor the spread of pulmonary tuberculosis. Probably an increase in the disease has not occurred to date in this country as a whole, but a rise has occurred among the belligerent nations and in some of our own industrial centers.

Increase in prevalence and mortality can be traced to inadequate diet, insufficient institutional facilities and medical care, lowering of resistance from apprehension and disturbed rest, and overcrowding and poor housing in centers of concentrated war industry.

Since the disease appears on the increase in countries at war for some time, it must be assumed a similar trend to be anticipated here. This calls for early diagnosis, hospitalization of active cases and discovery of infective contacts. Greatest hope for success lies in the interest and cooperation of the general practitioner. He sees the patient early and through his intelligent effort will come early diagnosis, prompt isolation and the investigation of contacts. Toward this goal a path is indicated for the practitioner, who, deprived of many a colleague, finds his problems multiplied and his strength and time in no wise reinforced.

Usually it is easy for a tuberculous specialist to make diagnosis once the suspect has been singled out by the practitioner. More difficult is it for the latter to give due consideration to tuberculosis—only one of many conditions that may assail his patient.

For example, cough is the commonest symptom of the disease. In one with a history of previous acute pleurisy, chronic cough is suspicious. Nevertheless, the disease may be present without it, and most agree that cough or any other symptom is a relatively later, not an encouraging earlier, manifestation of pulmonary tuberculosis. If

one persists in describing tuberculosis in terms of symptoms, one might as well omit further discussion of early diagnosis, even though it is admitted that knowledge of classic symptoms is essential if one is to have tuberculosis in mind when encountering those less fortunate cases long past the stage when early discovery was possible. These symptoms include fatigue, particularly in the late afternoon, loss of weight, low grade fever, chest pain and hemoptysis.

If tuberculosis is to be found preclinically or at onset of its earliest symptoms a thorough, practical and economical plan of attack is necessary. Weapons at hand include history, physical examination, tuberculin test, sputum examination, x-ray films and fluoroscopy.

Tuberculosis specialists generally believe that the greatest deterrent to early diagnosis by the practitioner is the expense of x-ray examination. If it were as easy to x-ray the lungs as to do a physical examination on many more early cases would be found. Where x-ray facilities are handy it is simpler to take a picture and study it than to do a physical examination which though thorough may fail to disclose the trouble. Most practitioners lack of nice x-ray facilities, but the truth remains there is no substitute for a good x-ray picture. Today, in all but the most rural communities arrangements can be made for x-ray films of the chest in the indigent as well as in others.

Physical examination may uncover rales, breath sound changes and so forth, but their absence does not mean absence of tuberculosis. In every sanatorium are patients with far advanced disease who have been told by their family doctors that no signs of tuberculosis were present. Similar oversight may occur in some early cases when symptoms are present as well as positive x-ray findings. This is no reflection on the skill of the physician but proves that symptoms and x-ray evidence are often present before definite physical signs of tuberculosis develop.

Fluoroscopy, even in the hands of experts is not so accurate as film methods in diagnosing tuberculosis. Serial pictures too, give better clues concerning the progress of lesions than does mere observation of the clinical record.

The tuberculin test variously conducted, is of value in the process of screening groups or studying individuals. A positive test shows that the skin has been sensitized by previous or present tuberculous infection. It does not prove that active pulmonary disease is present, but does call for an immediate x-ray film of the chest. A negative test, conversely, is almost conclusive that active tuberculosis does not exist. There are exceptions to this statement, but they are rare.

Sputum examination is vital. A positive sputum leaves no doubt that active disease is present, but a negative sputum is no guarantee of its absence. There may be relatively few bacilli in a sputum sample. Improper collection may provide saliva instead of thick material truly expelled from the lung by a spell of coughing or too few samples may be examined. Reinforcing the simple smear are concentration methods: culture or guinea pig inoculations, and examination of the fasting gastric sediment in those swallowing their sputum.

Tuberculosis cases should be reported promptly to the public health authorities who assist in determining their disposition.

Many practitioners are not interested in treating tuberculous patients. Others feel they see cases so rarely that they would welcome assistance by experts. Sanatorium care,

if available, promises conditions ideal for treatment and training of the patient and protection of his family and friends.

People who contract pulmonary tuberculosis usually do so because of intimate exposure to someone with a positive sputum. Thorough search is made in the patient's household and among his other associates, each being tuberculin tested and the positive reactors x-rayed. Obviously the x-ray film, if showing nothing at first, should be repeated at four-month intervals for several years, as breakdown may be slow to appear.

Many countries have well-organized tuberculosis associations whose nurses serve as fieldworkers. Granted this aid, the social side of the problem can be handled with personal home interviews and transportation of the patient and of the contacts to the sanatorium or clinic for testing and x-ray. Tuberculosis workers are well trained and function to give the practitioner able service and advice about the disposition of the case, in the adjustment of the family and in the follow-up of the patient once he leaves the sanatorium.

The family doctor should co-operate with those who have directed the treatment when he receives back the discharged case. Rehabilitation in these people is complex and important. Many sanatoriums have personnel specially trained to instruct patients in occupations they will be fitted to carry on after their cure, or to prepare them for the special problems facing them on their return to society. The family doctor must continue his interest through both treatment and rehabilitation periods, with periodic check-up, assurance and advice.

The greatest contribution the general practitioner can make in the field of tuberculosis in wartime is the intensification of his peacetime effort, keeping the disease constantly in mind and remembering that the ultimate ideal in controlling tuberculosis would be to have every adult x-rayed annually.—Reprinted from *Tuberculosis Abstracts*, April, 1943.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR FEBRUARY, 1943

DISEASES	FEBRUARY 1943	FEBRUARY 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	0	2	0
Chicken pox	1280	1651	1438
Diphtheria	9	11	12
Dog bite	520	474	531
Dysentery, bacillary	6	3	6
German measles	3490	261	80
Gonorrhea	345	326	326
Measles	2661	1753	1896
Meningitis, meningococcal	52	12	8
Meningitis, other forms	7	14	*
Mumps	1113	1930	777
Paratyphoid infections	3	4	2
Pneumonia, lobar	323	477	579
Scarlet fever	2081	1399	1002
Syphilis	363	374	405
Tuberculosis, pulmonary	177	223	179
Tuberculosis, other forms	16	14	21
Typhoid fever	3	6	5
Undulant fever	1	5	4
Whooping cough	658	779	779

*Pfeiffer bacillus meningitis only other form reportable previous to 1941.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

February, 1943

Diphtheria was reported from: Boston, 2; Chelmsford, 1; Fall River, 4; Foxboro, 1; Lowell, 1; total, 9.

Dysentery, bacillary, was reported from: Boston, 6, total, 6.

Encephalitis, infectious, was reported from: Pittsfield, 1, Somerville, 1; total, 2.

Lymphocytic choriomeningitis was reported from: Fort Banks, Winthrop, 1; total, 1.

Meningitis, meningococcal, was reported from: Adams, 1; Belmont, 1; Boston, 3; Brockton, 1; Cambridge, 1; Camp Edwards, 8; Chelsea, 1; Chicopee, 1; Everett, 1; Fall River, 1; Falmouth, 2; Fort Banks, 1; Fort Devens, 2; Hanson, 1; Holyoke, 1; Leominster, 1; Medford, 1; Newton, 2; Rehoboth, 1; Revere, 1; Salisbury, 1; Shrewsbury, 1; Somerville, 2; Spencer, 1; Stoneham, 1; Taunton, 1; Walham, 1; Warcham, 2; Webster, 1; Westover Field, 2; Weymouth, 1; Winthrop, 1; Worcester, 5; total, 52.

Meningitis, other forms, was reported from: Beverly, 1; Boston, 1; Newton, 1; Northbridge, 1; Woburn, 1; Worcester, 2; total, 7.

Paratyphoid fever was reported from: Salem, 1; Wakefield, 1; Westminster, 1; total, 3.

Septic sore throat was reported from: Amesbury, 1; Attleboro, 2; Boston, 1; Cambridge, 2; Newton, 1; Salisbury, 1; Swampscott, 1; Wakefield, 1; Winchester, 1; Worcester, 1; total, 12.

Trachoma was reported from: Boston, 1; total, 1.

Trichinosis was reported from: Boston, 1; total, 1.

Typhoid fever was reported from: Stoughton, 2; Wellesley, 1; total, 3.

Undulant fever was reported from: Southwick, 1; total, 1.

The trend upward of certain diseases, noticeable for several months past, continued during February. Meningococcal meningitis reached a record high for the month of February. Scarlet fever surpassed any February record since 1906, with the exception of that of 1927. German measles set up a new high February record.

Above the seven-year median figure were German measles, gonorrhea, measles, meningococcal meningitis, mumps, paratyphoid fever and scarlet fever.

Under the seven-year median were diphtheria (next to the lowest February record), lobar pneumonia (with a new low record for February), chicken pox, dog bite, syphilis, tuberculosis (both pulmonary and other forms), typhoid fever, undulant fever and whooping cough. There were no cases of anterior poliomyelitis reported during the month.

DR. PRATT DECORATED FOR VALOR

Lieutenant-Commander Theodore C. Pratt (MC), U.S.N.R., a member of the surgical staff of the Massachusetts General Hospital and of the Palmer Memorial Hospital (on leave of absence), has been awarded the Navy Cross "for extraordinary heroism and distinguished service in line with his profession as chief surgeon of a division field hospital on Guadalcanal." The citation states that Dr. Pratt courageously operated on and supervised treatment of casualties while the hospital was being bombed by enemy planes and shelled by surface craft during last August and September.

(Notices on page x)

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THE PHARMACEUTICAL MANUFACTURER AND ACADEMIC RESEARCH

FRANCIS BOYER*

PHILADELPHIA

UNTIL a few years ago, satisfactory co-operation in medical research between a commercial house and an academic research group seemed a definite impossibility. The academic group vividly remembered the pains and disappointments of what Dr John Stokes calls the "scrimmage era" of pharmaceutical manufacturing, and eyed commercial houses with "invincible distrust, aroused by admittedly distrust-deserving tactics in ultra distrustful minds."

As time went by, however, certain firms gradually expiated the sins of their fathers; and today a new relation in research is beginning to exist between the pharmaceutical manufacturer and the academic investigator. It has become evident that the first class commercial houses can be trusted, and that they have much to contribute to a research partnership.

Paradoxically enough, one advantage of the academic-commercial relation lies in the fundamentally different approaches of the scientist and the businessman to a given problem. The scientist is with few exceptions deeply, almost exclusively, immersed in his own specialty. Also, he is by temperament an intense individualist. Yet the increasing complexity of modern medical research makes teamwork and a knowledge and appreciation of contributing techniques ever more important. The businessman is essentially an organizer, working through human beings rather than in a specific science. His success depends on his ability to harmonize and dovetail the individual contributions of men who know more than he does, and this organizational approach is often as useful in research as it is in other fields.

This basic psychologic difference between scientist and businessman necessitates a real effort toward tolerance and understanding on both sides but without this difference the partnership would be less effective. In the co-operation of

manufacturer and academic research group, each contributes a mental make up that the other lacks, and this is one reason why the relation can be made a constructive one.

Moreover, the commercial house is organized to do many things that are difficult for an academic institution. For example, it can operate as a most valuable liaison agent, keeping in touch with those working on the same problem—perhaps with other clinicians, perhaps with workers in allied sciences. By its foreign contacts, it can secure information from other countries or obtain rare materials or new drugs. Its clerical force can furnish, without delay, skilled stenographic help, statistical assistance, library work and so forth, and can take in its stride the many "little jobs" that normally make such inroads into the scientist's time and energy.

* * *

Since the term "medical research" covers a wide field, it seems worth while to consider in some detail certain types of medical research that are especially adapted to academic-commercial collaboration.

Perhaps the commonest relation, and the simplest, is that involved in the clinical testing of a new drug. Let us suppose that the manufacturer has evolved a new compound and has carried through a preliminary study of its pharmacology and its toxicity in animals. He believes that it may be of value in the treatment of human disease and wishes to arrange for its clinical evaluation by an academic investigator.

A mutual understanding and appreciation must imbue this relation. Each partner must respect the contribution of the other. The manufacturer must realize that it will require much time and much money to test the new drug adequately, and to define its field of usefulness precisely. Until these steps have been completed he must firmly resist all pressure by his sales department to "jump-start" in marketing the product, or even to

* Present in the field of research. Smith, Moore & French, Labora-

publicize it on the side by premature or unauthorized references to the investigator's findings. The clinician, on the other hand, must not underestimate the difficulties—and the importance—of the chemical and pharmaceutical work done by the manufacturer's research staff.

Another fact that must be borne in mind by both parties is that, without a definite interest in the specific problem on the part of the investigator, satisfactory research cannot be obtained by mere money. The institution may be tempted to obtain funds for some needy department or for some worthy student. The manufacturer may be desperately anxious to have a particular study done. Yet, unless the project is of real interest to the investigator and to his department head, both manufacturer and institution will regret any arrangement they enter into. The scientist will have made the fatal mistake of working for financial assistance rather than for the intrinsic interest of the problem, and the commercial house will be extremely lucky to get even second-rate work. (Usually such a study bogs down and remains uncompleted, with apologies and guilty consciences on both sides!)

* * *

It is obvious that the academic group is invaluable to the commercial house for the clinical testing of promising compounds. Less well recognized is the fact that, in many clinical problems, the commercial house can give the academic group most useful chemical and pharmaceutical assistance. Unquestionably the ablest brains in pharmacology and clinical research are to be found in the universities. Conversely, many of the ablest chemists are employed by pharmaceutical houses. In addition, the laboratory equipment of commercial firms surpasses that of most universities, at least in the field of medicinal chemistry. The pharmaceutical manufacturer has the funds to buy, and as a competitive enterprise must buy immediately, the latest research equipment, whatever the expense.

Furthermore, in a commercial laboratory there is no interruption for teaching duties, no time out to prepare new courses. Much as the academic chemist might like to help out the medical department, he frequently cannot spare the time from his own departmental duties.

In short, the commercial house can lend to its academic partner first-class chemical—and pharmaceutical—brains, first-class equipment and undivided interest. Its assistance may begin in the very first part of the problem, when existing compounds need to be modified to avoid undesirable side effects or to obtain more intense action. Its greatest service, however, may very easily be in that difficult stage between test tube and mass

production, when the new drug is needed in sufficient quantities for large-scale clinical trial.

To implement this chemical assistance, it is often helpful for the manufacturer to establish a fellowship supporting a chemist, who becomes an integral part of the clinical research group and who also serves as a connecting link between that group and the manufacturer's chemical staff.

Again, the pharmacological testing of promising compounds is often a real problem for the clinical research group, and here, as in the case of chemistry, the commercial house can often provide assistance. Certain work may be clearly needed that the university department of pharmacology cannot carry out because of the press of teaching or a previous research commitment. In such cases, a fellowship from the commercial house may supply the additional man power needed, a grant for equipment may open up an annoying bottleneck, or the work may be done by the manufacturer's own pharmacologists.

* * *

The most obvious contribution of a pharmaceutical house to academic research is, of course, financial support. In these days of low interest rates and heavy taxation, universities are faced with reduced income from the gifts of individuals and even from foundations. More and more they must look for help either to a governmental agency or to commercial houses. Indeed, both these sources of income are needed if medical research is not to suffer.

Furthermore, quite evidently a way is being found by which commercial support can be received without hampering the search for scientific truth. In the old days, acceptance of commercial grants for research work automatically implied at least a taint of "commercialism." Today, a glance at the list of contributors to any leading medical school almost always reveals the names of pharmaceutical firms.

* * *

So far, a rosy picture has been painted of the academic-commercial partnership and of its advantages to medical research. It cannot be denied, however, that in this partnership there are definite difficulties that must be recognized and faced.

For example, the academic research group may seek the chemical co-operation of a manufacturer in developing a product that it—the university—has discovered. Is it fair for the manufacturer to gain large monetary rewards for the distribution of this product while the university receives none? On the other hand, are not patents by an academic body—however handled—likely to complicate, both practically and spiritually, its search for scientific truth? Again, in a really effective co-operative effort, there is always the like-

lihood that certain discoveries—perhaps improvements on the original idea—will be joint findings. Some will be patentable. To whom does the patent belong? Other discoveries may not be patentable. How shall they be handled?

One cannot answer these questions in any general terms. Much depends on the basic policy of the academic group. Equally important is the degree of its confidence in the particular commercial house, and this should grow, preferably, through a continued relation. Often the university does not realize the strength of its position. If one of its own scientists has discovered a compound, and university policy admits of patenting, it has a legal checkrein to control the standards of manufacture and marketing. And even when patent rights are joint, or technically belong to the manufacturer, the latter must either be guided by the university's wishes or jeopardize the very relation that has developed the product.

As a matter of fact, the importance of the actual letters patent is usually overemphasized. Few people realize that no patent can be considered more than presumptive until it has been adjudicated by the courts—and, incidentally, I believe that the Supreme Court has upheld only four patents in the last fifteen years. The research scientist is under the impression that a commercial house considers an exclusive patent a *sine qua non*, whereas in many cases all the manufacturer asks or needs in his marketing is a head start over competitors. He naturally secures this start if he has been closely associated with the product's development, but he retains his advantage only during good behavior. If his prices are too high, if he neglects possible improvements, competition overtakes him.

In the academic-commercial partnership, therefore, it is not impossible to work out a satisfactory solution to patent questions, even though each instance presents an individual problem. More important than legalities and contracts is the factor of mutual confidence. Without this, no formal patent policy can be wholly satisfactory. With it, a sound handling of patents can almost always be achieved.

* * *

Of less fundamental importance than the patent problem, but at times productive of a strain on the academic-commercial relation, is the question of when and on what basis grants should be terminated. In certain cases it is possible to agree in advance on a definite grant for a specified term. Even so, the wise manufacturer mentally sets aside a certain sum each year for necessary expenses that cannot be foreseen. Furthermore, he will not be too disturbed if, at the end of the period originally fixed, a research project is like

a house with its walls all built but no roof, necessitating an extra year's grant to prevent the preceding work from being wholly lost.

Most research problems, however, are distinctly indefinite from the beginning. The association between university and manufacturer just grows, and grants grow with it. A particular project of mutual interest is started. The commercial house pays the salary of a young physician who is to work under the chief clinical investigator. Results are encouraging. Later the commercial house supplies a chemist. Next, a couple of technicians are added.

All this is perfectly satisfactory while active study in the chosen field of mutual interest is going forward. But the day inevitably comes when the particular project is at an end. It may have resulted in a new compound, marketed by the commercial house. Or it may have proved unproductive, and the interest of the research group may have been diverted to quite different fields, fields in which a pharmaceutical house—or the particular firm—can make no foreseeable contribution.

For how long, in such a situation, should the commercial house continue its grant? Here, as in the case of patents, there is no hard and fast rule. But if certain lines of thought are adhered to—and, if possible, put down on paper at the start—strain on the relation can be greatly eased. As a cardinal principle, all grants should be made with a clear understanding that they will be rediscussed at a time sufficiently in advance of their termination to allow all concerned to make suitable plans for the future. If the original grant was for more than a year, this discussion should take place at least a year before the termination date.

Furthermore, there should be a fundamental distinction between the general support of a research group—or of an individual investigator—and the supplying of technical assistance for a specific project. It is entirely reasonable for those in charge of a commercial house to support a major investigator, even though he is working on a project that is of no immediate interest to them. They may be grateful to him for past help. They may hope that later on he will turn to work that is of interest, or they may believe that he is a man of outstanding ability, whose efforts should be encouraged on general principles.

But grants for technicians are on a somewhat different basis. Although the commercial house can well be expected to supply technical help for a project of interest to it at the time, it is scarcely reasonable to expect this support to continue after the conclusion of the specific problem. Yet technicians easily drift into a more or less permanent status on a department's staff, and subsequent

withdrawal of financial support, unless it has been anticipated, will dislocate the whole organization.

* * *

Probably the most complicated form of academic-commercial relation is an association over a considerable period of years between an academic research group and a manufacturer. But it is also the one most likely to yield maximum benefits.

In modern medicine there is a growing realization, as President Conant of Harvard University has put it, that if research is to progress "only a group can furnish the collective ability required: the chemist transforming one drug to another; the pharmacologist studying its fundamental action on animals and man, and the clinical investigator bringing his knowledge of the actual problems of therapeutics—all these must join hands and pool their ideas."

Selected commercial houses can well be made a part of this team, not only to give assistance in the actual research work, but also to translate the results of that research into practical clinical application. After all, an academic research group has been working in a vacuum unless its findings are eventually made available to the medical profession as a whole. Where a new drug is involved, this can only mean that *some* manufacturer must advertise and distribute it. And much is gained if this manufacturer is one who has demonstrated his integrity and his qualifications through past collaboration.

It is, of course, possible for a scientist merely to announce his discovery and leave its commercial aspects open to competition. But this almost inevitably results in a hasty, unsupervised rush for the market, with a consequent loss of the service that a preselected manufacturer can perform—not only in research, but also in marketing the product under the guidance of the academic group.

Frequently the research scientist does not appreciate the gulf between his own specialized field and the daily work of the average practitioner. For a new drug to be properly utilized, it is not enough for its discoverers to know, however thoroughly, its indications, effects and limitations. They must also know the viewpoint of the average practitioner, his diagnostic facilities and the conditions actually encountered in his practice. Precisely this information is revealed by the manufacturer's field investigations.

Although pharmaceutical advertising should not usurp the function of medical teaching, it can be made a great force for good. It is infinitely more constructive for leaders in medicine to direct this force than for them to dismiss it as "mere advertising." To disseminate knowledge

of a new therapeutic agent accurately and effectively, manufacturer and scientist must co-operate. Sympathetic scientific guidance can raise the whole standard of pharmaceutical marketing.

When the Duc d'Enghien was executed, Fouché, Napoleon's minister of police, remarked, "It was worse than a crime, it was a blunder." In the same sense, a commercial house must be stupid as well as unscrupulous to cut its own throat by distorting an investigator's findings in an effort to present a favorable advertising picture. Actually no one has more at stake than the manufacturer in obtaining and disseminating the true facts about his product. No one is so hurt when the results in actual practice fall short of the promises made. The physician who writes an overenthusiastic paper suffers in reputation alone. But the manufacturer who puts out exaggerated advertising almost always eventually suffers not only in reputation but in pocketbook as well.

Not only in research but in the actual marketing of his products, a farsighted manufacturer appreciates that he has much to gain by real sincerity in his co-operation with an academic group. To make the relation a commercial success—even if this is his only criterion—the manufacturer must give to medical science more than lip service. From the merest self-interest he must take the long-range point of view and sacrifice immediate commercial gains for the advancement of medicine and the trust and confidence of his university partner. Thus, in almost any difference of opinion with the academic group, he, the manufacturer, must be the one to yield.

In short, although their approaches to a given problem may seem diametrically opposed, the true interests of the research worker and the manufacturer are in reality similar. Clinical and commercial values are almost always identical. A drug that has merit is virtually certain to be a financial success. A drug that fails to fulfill the claims made for it is likely to be a costly enterprise, a sinkhole into which advertising and sales money are poured. It requires neither a truism nor genius on the part of the manufacturer to realize that "honesty is the best policy."

* * *

In developing a new drug and establishing its use by the profession, a number of separate steps must almost always be taken: chemical synthesis or modification, animal pharmacology, human pharmacology, clinical testing and general marketing. It is more and more evident that neither manufacturer nor university can effectively handle all these steps without the help of the other. If the best interests of both are to be served, they must work together to eliminate the last remaining barriers to their collaboration.

ACUTE APPENDICITIS IN PATIENTS WITH THE COMMON CONTAGIOUS DISEASES

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THE records of patients admitted to the Willard Parker Hospital for Contagious Diseases between January 1, 1935, and April 1, 1941, were reviewed for the concomitant incidence of acute appendicitis. In a high percentage of these cases, the appendix was already gangrenous or ruptured. Apparently diagnosis and surgical intervention had been delayed. This may be attributed to the presence of rash or other stigmas of the contagious diseases that tend to deflect the physician's attention from the abdomen. Although it is true that nonappendiceal abdominal symptoms are common during the course of the various communicable diseases, this fact should not deter one from diagnosing acute appendicitis if there is sufficient evidence.

The incidence of appendiceal disease in the cases comprising this study is given in Table 1.

TABLE 1. Incidence of Appendicitis in Various Contagious Diseases.

DISEASE	NO. OF CASES	CASES OF APPEN- DICITIS	INCIDENCE %
Measles	8,997	24	0.27
Varicella	3,576	8	0.21
Scarlet fever	9,079	9	0.09
Mumps	1,685	8	0.47
Pertussis	3,064	3	0.09
Rubella	816	1	0.12
Diphtheria	1,985	0	0.00
Totals	29,802	53	
Incidence			0.18

Only cases in which there was gross and microscopic evidence of acute inflammation of the appendix are included.

MEASLES

Only one of the standard textbooks on infectious diseases¹ describes appendicitis as a complication of measles, and that one briefly. The authors emphasize that suppuration at any stage is rare, and that temporizing is the wisest course when abdominal pain occurs during the invasive period of measles. That this neglect of an important subject has taken its toll is evidenced by the number of patients with far-advanced appendicitis admitted to the Willard Parker Hospital.

The classic report by Panum and Manicus of a measles epidemic on the Faroe Islands in 1846

describes a syndrome that strongly suggests appendicitis and its complications. At this period, acute appendicitis was not recognized as a clinical entity. The authors speak of two types of measles, the catarrhal and the gastric. The latter was characterized by colicky abdominal pains, high fever, tense rigid abdomen tender to pressure, diarrhea and vomiting. Some of the patients died, whereas others made slow recoveries. The symptoms came on early, either before or after the rash appeared.

Thenebe, Hirschberg and Cencr² in 1933 reported 6 cases of appendicitis among 371 measles patients admitted to the Hartford Isolation Hospital. In 1936 Hudson and Krakower³ described 8 cases of acute appendicitis during the course of measles. Bullova, McCabe and Wishik,⁴ also reporting from the Willard Parker Hospital, have summarized 11 cases of appendicitis occurring among 6357 measles patients treated during the five years preceding our survey. Accounts of other cases in the literature^{5, 10} do not lend themselves well to tabulation. They differ little from those in our report. We found 24 cases of acute appendicitis (0.27 per cent) among 8997 patients with measles admitted to this hospital. Combining our figures with those of Bullova et al, there were 35 cases (0.23 per cent) among 15,354 measles patients admitted during a ten-year period. Included in Tables 2 and 3 are the statistics from these 35 cases as well as those from 29 similar cases taken from the literature, which make our analysis more conclusive. Also mentioned in the literature, but not included in our statistics, are 8 measles patients from whom normal appendices were removed because of abdominal symptoms.

The appendicitis cases listed in Tables 2 and 3 fall in the age group between three and twelve years, averaging from five to eight years. In our own series males outnumber females by 21 to 3. In the collected group there are 37 males and 16 females, in spite of the fact that both sexes are about equally susceptible to measles. Fischer⁷ reported 2 perforated cases, one in a girl of fourteen, the other in a boy of seventeen. Popper reported 1 case in a twenty-six-year-old man. Other single cases reported have been in children under eight.

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Onset

Appendicitis complicating measles apparently tends to occur during the invasive and catarrhal period of the disease—from six days before the

as our own. From these figures it can be seen that the white-cell counts and differentials in acute appendicitis complicating measles are about the same as they would be without the

TABLE 2. Acute Appendicitis Complicating Measles: Perforated Cases.

CASE No.	AGE	SEX	INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND RASH		INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND OPERATION	WHITE-CELL COUNT	POLY-MORPHO-NUCLEAR LEUKO-CYTES	COMPLICATION
			BEFORE	AFTER				
	yr.		days	days	days		%	
Willard Parker Hospital, 1935-1941								
1	5	F	5		2	13,000	80	General peritonitis
2	5	M		4	0	19,800	86	Local abscess
3	6	M		2	1	17,000	88	General peritonitis
4	7	M	2		2	9,100	88	Local peritonitis
5	7	M	Same day		4	14,250	94	General peritonitis
6	6	M		2	2	22,450	85	General peritonitis
7	7	F		2	1	10,800	91	General peritonitis
8	4	M		3	2	28,800	86	General peritonitis
9	3	M		2	4	16,300	83	General peritonitis
10	5	M	2		3	15,500	84	Local peritonitis
11	4	M	5		2			Local abscess
12	6	M	Same day		2	13,250	84	Local abscess
Thenebe, Hirshberg and Cenci ²								
1	5	M		12	2			Local abscess
2	5	M		2	1	14,300	80	General peritonitis
3	5	F		1	1	9,400	79	Local abscess
4	6	M	Same day		16	40,000	92	Pelvic peritonitis with abscess
Hudson and Krakower ³								
1	7	M	Same day		8			Appendiceal abscess
2	8	F	Same day		11			Appendiceal abscess
3	6	F	1		2			Suppurative; local abscess.
4	9	M		4	13			Appendiceal abscess
5	7	M		3	7			Appendiceal abscess
6	6	F		2	1			Local abscess
Bullocka, McCabe and Wishik ⁴								
11 cases with local or generalized peritonitis								
Sex: 4 males, 7 females								
Age: 3-8 years								
White-cell count: 12,000-21,800, with 76-89 per cent polymorphonuclear leukocytes								
Time of onset:								
			BEFORE RASH		AFTER RASH			
			NO. OF CASES	NO. OF DAYS	NO. OF CASES	NO. OF DAYS		
			1	5	1	1		
			1	6	2	2		
					2	3		
					2	4		
Interval between onset of abdominal pain and operation: 2, 4, 5 and 6 days								
Deaths: 2								

rash to four days after its appearance. Contrary to general opinion, appendicitis may occur in the prodromal stages and at the onset of the eruptive stage as frequently as it does after the rash is already established. In the collected series, 19 cases had their onset during the prodromal stage, 7 occurred on the same day as the rash, and 27 developed after its appearance.

In practically all our cases, white-cell counts and differentials were made just before the operation. The statistics shown in Table 4 were compiled from cases in the literature, as well

underlying contagion. In uncomplicated measles there is a leukopenia supposedly due to depression of the bone marrow with consequent relative lymphocytosis.

In general, with the usual exceptions,^{6,7} the white-cell count and differential are of some value in determining whether the appendix has been invaded by pathogenic organisms. Given a patient with a known exposure to measles, no rash, respiratory and abdominal symptoms, indefinite appendiceal signs and a low leukocyte count, it is fairly safe to assume that one is dealing with

pseudoappendicitis. This is the type of case, however, that must be observed carefully for signs of progression.

Table 2 lists 33 cases in which the appendix was perforated before operation. Twenty-six of these

leave the appendix because of difficulty in removing it without spreading infection, although at times this is a wise procedure. Drains were used in the presence of peritonitis or cloudy fluid. Blood transfusions, Wangenstein apparatus and mor-

TABLE 3. *Acute Appendicitis Complicating Measles Unperforated Cases*

Case No	AGE	SEX	INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND RASH		INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND OPERATION	WHITE CELL COUNT	POLY MORPHO NUCLEAR LEUCOCYTES %	TYPE OF ACUTE APPENDICITIS
			BEFORE	AFTER				
	yr.		days	days	days			
Willard Parker Hospital, 1935-1941								
13	12	M		2	2	10 000	75	Suppurative
14	10	M	6		0	13 800	82	Not stated
15	5	M		4	0	9 850	81	Gangrenous
16	12	M	3		1	14 000	78	Gangrenous
17	7	M	1		1	8 550	80	Suppurative
18	6	M		3	1	13 000	90	Suppurative
19	7	M	Same day		0	10 050	82	Suppurative
20	10	M		2	2	13 600	89	Suppurative
21	5	F	3		1	14 200	87	Suppurative
22	5	M	4		1			Gangrenous
23	8	M	3		2	19 600	80	Not stated
24	6	M	1		0	11 000	79	Not stated
Thenebe Hirschberg and Cenci ¹²								
5	6	F	2		2	10 000	82	Gangrenous
6	6	M	1		1	12,400	86	Catarrhal
Davidsohn and Mori ¹¹								
1	6	M	4		1	17,000	77	Gangrenous
2	8	M	Same day		2	12 000	82	Suppurative
3	6	M	3		1	12,500	82	Suppurative
4	7	M		8	1	9 600	76	Suppurative
Hudson and Krikower ¹³								
7	9	F	3		1			Not stated
8	6	M		3	0			Not stated

cases developed during the stage of eruption. There was an average wait of four days between the onset of abdominal symptoms and operation, in the perforated cases, and an average wait of one day in the unperforated ones (Table 3). This does not indicate that appendicitis is more virulent when it arises in the eruptive stage, but rather demonstrates how the presence of a rash leads to delay in diagnosis.

In all the ruptured cases in our series except 1, the appendix was perforated before admission and while the patients were under the observation of a physician. This indicates that lack of familiarity with this complication leads to unwise procrastination.

The treatment for this complication of measles is exactly the same as that for appendicitis under any other circumstances. Operation in our series was performed as soon as a positive diagnosis was made, except in a few cases where dehydration and acidosis were first relieved with parenteral fluids. In only 1 case was it necessary to

plume were used freely when indicated. Chemotherapy was tried in a few cases, but the results were inconclusive. Measles convalescent serum

TABLE 4. *White-Cell Counts and Differentials in Cases of Appendicitis Accompanied by Measles.*

CONDITION	NO. OF CASES	WHITE-CELL COUNT		POLY MORPHO NUCLEAR LEUCOCYTES %
		RANGE	AVERAGE	
Appendix inflamed but still intact	17	8 500-19,000	12 450	60-60
Appendix perforated with abscess or peritonitis	27	9 000-28 800	15 900	76-74
Pseudoappendicitis	9	2 350-15 000	7 410	41-53 (avg. 72)

was given intravenously to a highly toxic prodromal measles patient with a ruptured appendix and abscess. This patient, already showing Koplik's spots, had a rapid temperature drop to normal and mild rash, and was thought by several competent observers to have a noticeable general improvement.

Nitrous oxide and oxygen, ether and cyclopropane were the commonest forms of anesthetic employed. Two patients developed pneumonia postoperatively within two weeks of each other in 1935, but since then there have been no respiratory complications. We are of the opinion that general anesthesia is relatively safe during any stage of measles.

We found 8 cases in which the appendix did not show enough disease to warrant its surgical removal. All the cases occurred in children between the ages of six and ten, except for 1 atypical case that occurred in a patient seventeen years old. Boys and girls were equally affected. These cases occurred only in the six days preceding, or simultaneous with, the onset of the eruption. Appendiceal symptoms coming on after the exanthem had appeared were never due to pseudoappendicitis. The leukocyte counts were for the most part normal, averaging 7410 but ranging from 2250 to 15,000. There was some evidence of an increase in the neutrophils, with an average percentage of 72. In 5 of the above cases, microscopic examination of the appendix revealed lymphoid hyperplasia.

The degree of severity of measles is apparently no indication of which case will develop suppurative appendicitis. Some of our patients had a mild form of the disease. When the patient has been exposed to measles, and at a reasonable interval develops abdominal pain, the physician should be alert to the two possibilities: benign pseudoappendicitis and true acute appendicitis.

The earlier belief that the postoperative course is particularly severe after measles is not based on fact, since our patients all made fairly rapid recoveries commensurate with the amount of abdominal disease present. There were no pelvic abscesses, fecal fistulas or cardiac decompensations, which were said by Rost⁸ and others^{9, 10} in the German literature to be common in these cases. Two patients in our series developed pneumonia but made rapid, uneventful recoveries.

The diagnosis of pseudoappendicitis is a difficult one and we can only offer the following suggestions. Abdominal pain, nausea and vomiting come on during the six pre-eruptive days or simultaneously with the rash. The abdominal signs more often than not are vague, and disappear when the rash is well established. The white-cell count as a rule is normal or low. The patient is usually six to ten years old. Temperature is of no aid as a differentiating point, since it may be similar to that in true appendicitis. The important point to remember is that when observation is thought necessary, the patient should be seen several times rather than once a day. If definite

signs of appendicitis are present, immediate surgery is indicated regardless of coexisting signs of measles. The postoperative course in the pseudoappendicitis cases was mild and uneventful. Therefore, it is better to operate in questionable cases than to run the risk of appeasing an inflamed appendix.

It is impossible, on the basis of our study, to make a definite statement as to whether the relation between measles and appendicitis is more than coincidental. There are, however, certain facts that justify speculation.

One theory is that the lymphoid hyperplasia of measles, with or without catarrhal enteritis, sets up a chain of circumstances leading to interference with drainage and circulation in the appendix and resulting in secondary invasion by bacteria. The evidence in support of this theory lies in the fact that measles causes a moderate hyperplasia of the lymphoid tissue throughout the body, and that this is often especially well seen in the appendix that is richly endowed with lymphoid structures. Hwang and Krumbhaar¹² have demonstrated that the percentage of lymphatic tissue in the appendix is greatest in the ages between one and ten and that the female appendix contains less lymphatic tissue than the male throughout life. In the light of this work, the preponderance of males over females in our series (21 to 3) fits in well with the above theory.

Nausea, vomiting and localized pain in the right lower quadrant often accompany the catarrhal symptoms at the onset of the invasive stage of measles. These abdominal symptoms coming on in the period six days before the rash constitute the so-called "pseudoappendicitis syndrome," and may represent an actual distention of the appendix from the lymphoid overgrowth that is frequently described in microscopical descriptions of these appendices. Hudson and Krakower's³ findings do not substantiate this theory. They compared microscopic sections from their 8 cases of appendicitis during measles with some from children in whom measles was not present. There was less lymphoid tissue, with practically no secondary centers or germinal follicles, in the group with measles, and there appeared to be more plasma cells. Because of the anatomical variations in the two groups, the authors were of the impression that the association of measles and appendicitis is more than coincidental.

The abdominal symptoms in the invasive stage usually subside when the rash appears. This may be due to exhaustion of the lymphoid reaction. However, if the physician is not alert to the fact that a certain number of these cases go on to suppuration, he will err in his diagnosis. The

tendency to devalue abdominal symptoms because a child is thought to be incubating measles is illustrated in the following case reported from this hospital.¹³ A child with abdominal pain was treated with laxatives for five days because she was apparently in the prodromal stage of measles. She died within an hour of being admitted to the hospital. Post mortem examination revealed a ruptured appendix with generalized peritonitis. The case is not included in our statistics because the patient died before the rash appeared. A study of the cases in our series disproves the popular belief that the abdominal symptoms in the prodromal stage are due to mesenteric adenitis alone and always subside with the onset of the rash.

If one accepts the popular belief that the pathogenic agent in measles is a filterable virus present in the blood and nasal secretions, another theory suggests itself. There is evidence that the invasive and injurious action of measles is not restricted to the eyes, skin and respiratory tract but may involve other parts of the body, including the tissues of the appendix.^{14, 15} Herzberg¹⁶ in 1932 reported for the first time the presence of Warthin-Finkeldey^{17, 18} giant cells in an appendix removed during the prodromal stage of measles. Davidsohn and Mora¹¹ in 1932 described 4 measles cases in which appendectomy had been performed. In 2, the appendix was removed two days before the rash was noticed, and microscopic study revealed many giant cells. In 1, in which the appendix was removed two days after the rash appeared, there were few giant cells. The fourth case, in which the appendix was removed nine days after the onset of the rash, had no giant cells. Case reports similar to these have been made by other authors.^{3, 4, 19, 23} Reports from the hospitals where appendectomy was performed on our prodromal cases made no mention of the presence of giant cells.

The described cells are large, round or irregular shaped, with much eosinophilic or basophilic cytoplasm. There may be from three to fifty round, lightly staining nuclei characteristically clumped together in the center of the cell. Giant cells are found in various locations throughout the body, and occasionally only in the lymphoid tissues and mucosa of the appendix. These cells when found during the prodromal stage of measles are now generally recognized as a specific reaction to the measles virus or its toxin. Further evidence that the appendix may be involved directly by the measles virus is the recent finding of inclusion bodies in this organ by Broadhurst, McLaren and Struening.²⁴

This problem could be further investigated by inoculating monkeys with an emulsion of an appendix removed from a prodromal measles patient and attempting to demonstrate giant cells in the lymph nodes of the experimental animals, similarly to the recent transmission experiments of Gordon and Knighton.²⁵

Is it possible, then, that if the virus does reach the appendix, it traumatizes this organ sufficiently to cause a "virus appendicitis," which may predispose the tissue to further invasion by bacterial organisms? This view suggests that a better name for pseudoappendicitis is benign virus appendicitis, and that the prodromal abdominal symptoms of measles are often due to an actual appendiceal inflammation of virus origin. An appendix that was the seat of previous inflammation or one that harbored a fecolith would be especially vulnerable to attack.

VARICELLA

Varicella is an acute infectious disease with mild prodromal constitutional symptoms, and is the least dangerous of the various exanthematous diseases with regard to serious secondary lesions and mortality. The commonest complication is skin infection, secondary to scratching of the varicellous lesions. Abdominal disease developing during the course of the disease is rare.

Bullowa and Wishik,²⁶ on summarizing 2534 cases of varicella, found that appendicitis was the only abdominal complication. They reported 5 cases, an incidence of 0.19 per cent (Table 5).

TABLE 5 *Acute Appendicitis Complicating Varicella (Bullowa and Wishik²⁶)*

Case No.	Interval Between Onset of Abdominal Symptoms and First Rash		Interval Between Onset of Abdominal Symptoms and Last Rash		Type of Appendicitis
	Pre-rash days	Post-rash days	Pre-rash days	Post-rash days	
1	?	?	3	?	Perforated with localized peritonitis
2	1	?	?	?	Gangrenous and perforated with localized peritonitis
3	1	1	1	1	Not stated
4	3	3	6	6	Gangrenous and perforated with abscess
5	4	4	1	1	Gangrenous and perforated with localized peritonitis

From 1935 to 1941, 8 in 3576 admissions, an incidence of 0.21 per cent, were admitted to the Wilbur Parker Hospital. They are described in Table 6.

Abdominal pain is an extremely rare complaint during the prodromal and eruptive stage of varicella, and its presence should suggest the possi-

bility of appendiceal disease. Appendicitis may occur at any stage of the disease. In the 13 cases from the Willard Parker Hospital, 8 had their onset in the five days before the rash, and the rest

eral anesthesia was used without complications in any case.

In the cases operated on before the rash appeared, it is interesting to note that the first vari-

TABLE 6. *Appendicitis Complicating Varicella (Willard Parker Hospital, 1935-1941).*

Case No.	INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND RASH		INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND OPERATION	WHITE-CELL COUNT	POLY-MORPHO-NUCLEAR LEUKOCYTES	TYPE OF ACUTE APPENDICITIS
	BEFORE	AFTER				
	days	days	days		%	
1		9	0	20,600	96	Gangrenous
2		7	2	27,800	94	Suppurative and perforated, with general peritonitis
3		2	3	16,500	82	Suppurative and perforated, with abscess
4	4		3	16,040	88	Suppurative
5	5		0	28,200	97	Suppurative and perforated, with peritonitis
6	4		0	20,500	86	Not stated
7	3		0	9,000	78	Gangrenous
8	4		1	14,000	83	Gangrenous

in the nine days following its first appearance. The signs and symptoms in all cases were classic for acute appendicitis. In 3 cases, the diagnosis was made more difficult because of coexisting pharyngitis. The leukocyte counts ranged from 7800 to 28,000, with 79 to 96 per cent polymorpho-nuclear leukocytes.

In 10 cases (76 per cent), the appendix was either gangrenous or ruptured, with cloudy or purulent peritoneal fluid.

It is interesting to note that delay in surgical intervention was commoner in the erupted cases than in the nonerupted.

There is no evidence that there is anything but a coincidental relation between varicella and ap-pendicitis. Johnson²⁷ described a complete post-mortem examination of an infant who died dur-ing the height of the eruptive stage, and reported the appendix as being normal. Tomlinson²⁸ re-ported a case of varicella developing three days after tonsillectomy, in which microscopic exam-ination of the tonsils showed giant cells resembling those described as occurring during the prodromal period of measles. In 2 of our cases, the appendix was removed during the prodromal stage of vari-cella and showed histopathological evidence of acute inflammation, but no giant cells were found. Since the skin lesions of varicella may become infected and produce a secondary septicemia, the blood stream may serve as a route to precipitate acute appendicitis. However, none of our cases were complicated by severe skin infections or sep-ticemia. As in some of the other contagious diseases, the low incidence of appendicitis makes it appear that it was a coincidental complication of varicella rather than a direct result of it.

The course of varicella was not modified by appendicitis. There was no specific therapy. Gen-

cellous lesions often appeared under the adhesive tape over the abdomen.

SCARLET FEVER

The usual complications of scarlet fever are otitis media, sinusitis, cervical adenitis, mastoid-itis, arthritis and nephritis. Abdominal complica-tions occur infrequently and consist of enteritis, mesenteric lymphadenitis, toxic hepatitis and pri-mary peritonitis. Appendicitis is rare, and ac-cording to Dick and Dick²⁹ does not warrant dis-cussion.

Brandman,³⁰ who collected 39 cases from the literature, believes that more emphasis than at present should be placed on appendicitis as a com-plication of scarlet fever. He adds that it occurs more frequently in scarlet fever than in mumps, measles, varicella or tonsillar diseases. Kauffman³¹ claims that the appendix is constantly involved in scarlet fever, and that this accounts for the vomiting and abdominal pain. Bullowa et al.⁴ de-scribed 3 cases of appendicitis complicating scar-let fever among 6252 patients. Rolleston and Ron-aldson¹ mention 2 similar cases occurring late in the disease. Toomey³² lists this complication as being present in 9 of 6000 cases of scarlet fever. Thenebe³³ reported 4 cases of appendicitis among only 250 patients admitted with scarlet fever.

During the last five years there have been ad-mitted to the Willard Parker Hospital 9679 cases of scarlet fever, with acute appendicitis compli-cating the picture in 9 cases, an incidence of .09 per cent (Table 7). This does not include 10 cases admitted during the same period in which the rash appeared postoperatively. The latter we have considered as surgical scarlet fever and have omit-ted from this study. Two cases were excluded al-though operation revealed abscess formation in the

right lower quadrant of the abdomen, because the appendix was not found. The cases reported in the literature are similar to ours, and no further information would be furnished by tabulating them.

Abdominal pain is not a common symptom during the early or late stages of scarlet fever,

gangrenous and in another it had ruptured. In our series there were 2 deaths resulting from ruptured appendix with peritonitis. In one case surgery was not performed until the second day after the onset of abdominal pain, and in the other not until the fourth day. However, in 5 cases operated on comparatively early, that is, within thirty-six

TABLE 7 *Appendicitis Complicating Scarlet Fever (Willard Parker Hospital 1935-1941)*

Case No	INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND RASH		INTERVAL BETWEEN ABDOMINAL SYMPTOMS AND OPERATION	WHITE CELL COUNT	PERI- APIC- ULUS LEUKO- CYTOSIS	TYPE OF ACUTE APPENDICITIS
	BEFORE					
	days	AFTER days	days			
1	Same day		1	11 350	81	Not stated
2	Same day		2	13 500	8	Gangrenous
3	Same day		1	22 500	82	Not stated
4	2		4	8 500	8	Not stated
5		1	4	30 900	84	Suppurative and perforated with peritonitis fatal
6		4	2	36 200	94	Gangrenous and perforated with peritonitis fatal
7		12	Same day	13 450	82	Not stated
8		19	Same day	19 350	83	Gangrenous
9		19	1	20 500	85	Not stated

but nausea and emesis are present in 60 to 80 per cent of the cases. The vomiting rarely persists through the prodromal stage unless complications have already developed. The complaint of abdominal pain during the prodromal, eruptive or convalescent stage should not be taken for granted as being of the referred or secondary type until abdominal disease has been ruled out. In the cases from the literature and our own series, the abdominal pain was a prominent symptom that developed anywhere from the day of eruption to the twentieth day of the illness. Only 1 of our 9 patients complained of abdominal pain before the rash appeared, and in this case it persisted into the eruptive stage. Three patients had the onset of symptoms the same day the eruption was noticed. The remaining 5 patients complained of abdominal pain at intervals varying from the first to the nineteenth day after the scarlatinal rash. The signs and symptoms in practically all these cases were typical of acute appendicitis. There was nothing remarkable about the blood picture. The usual leukocytosis of scarlet fever was found, and the higher counts were found with complicated appendicitis cases.

As has been emphasized before, there is a tendency to delay surgical intervention in the face of obvious abdominal signs when scarlet fever complicates the picture. When in doubt it is wiser to operate, for patients who are operated on late may die of peritonitis. There were 9 perforated appendices, an incidence of 23 per cent, in the series compiled by Brandman.³⁰ Of the 4 cases reported by Thenebe,³³ in one the appendix was

hours after onset, a gangrenous appendix, which was unruptured, was found in only 1.

During the period studied there were also admitted to this hospital 10 postoperative appendectomy cases complicated by scarlet fever. In 8 cases the rash developed two to seven days postoperatively. These are classified as surgical scarlet fever cases. Brandman had 3 similar cases that he included in his series. He suggests that the abdominal symptoms were due to scarlet fever rather than to acute appendicitis. It is interesting that in 4 of our so-called surgical scarlet fever cases, appendices were reported as being of the chronic type, while the others showed evidence of acute inflammation. There were no ruptured or gangrenous appendices in this group. It should also be noted that 6 of these patients developed infected incisions, whereas only 1 of the patients operated on after the eruption had occurred did so.

There is no characteristic pathologic picture of the appendix removed during the prodromal, eruptive or convalescent stage of scarlet fever. Appendicitis does not modify the course of the disease.

Treatment in our series consisted of surgical intervention once the diagnosis was made. Nitrous oxide, oxygen and ether was used during the catarrhal stage without producing additional complications. The use of antitoxin did not prevent appendicitis. Chemotherapy and scarlet fever convalescent serum were employed in a few postoperative cases, and although they appeared to benefit the patient, no definite statement can be made because of the small number of cases.

Brenneman³⁴ claims that it is conceivable that organisms producing nose and throat infections travel to the appendix by the hematogenous or enteric route. Kojis and McCabe,³⁵ reporting on primary peritonitis complicating scarlet fever, tend to discredit but do not disprove the hematogenous route as the source of peritonitis. They found

The first case of appendicitis occurring during the course of epidemic parotitis was described by Simonin³⁸ in 1903. Dick³⁹ in 1935 stated that there was an increase in the incidence of appendicitis during mumps epidemics. Sneierson⁴⁰ in 1940 reported 2 additional cases. At the Willard Parker Hospital during the five-year period cov-

TABLE 8. *Mumps Complicated by Appendicitis.*

SOURCE	CASE No	AGE	SEX	INTERVAL BETWEEN PAROTID SWELL- ING AND ABDOM- INAL SYMPT- OMS	INTERVAL BETWEEN ABDOM- INAL SYMPT- OMS AND OPERA- TION	WHITE- CELL COUNT	POLY- MORPHO- NUCLEAR LEUKO- CYTES %	TYPE OF ACUTE APPENDICITIS
				days	days			
Benassi ⁴²				5				Perforated, with generalized peritonitis
Sandler and Finne ⁴¹				5		12,150	84	Perforated
Finch ⁴²				5				Perforated, with abscess
Donnelly and Oldham ⁴³				7	4			Gangrenous, and perforated
Seelye ⁴⁴		6	F	4	0	14,200	76	Gangrenous
Willard Parker Hospital	1	12	F	4	1	21,250	90	Gangrenous, with abscess
	2	16	M	6	1	14,000	81	Gangrenous
	3	19	M	10	1	11,000	75	Not stated
	4	12	F	5	3	13,700	81	Gangrenous
	5	14	M	9	0	19,500	82	Gangrenous
	6	7	M	4	1	20,000	79	Gangrenous
	7	9	M	5	1	13,000	81	Gangrenous
	8	5	M	3	1	18,000	92	Gangrenous

that out of 42 cases of scarlet fever with streptococcemia, only 1 had generalized peritonitis at autopsy. There is also no final evidence that the enteric route serves to spread the infection. Kunzel³⁶ found that his cultures of the appendix and intestines were sterile, whereas peritoneal and nasopharyngeal cultures grew streptococci. Another view, suggested by Thenebe,³³ is that the toxemia of this disease may have a special affinity for, or lower the resistance of, the appendix, making it more susceptible to invasion by the colon bacillus. Autopsies of scarlet fever cases usually show a generalized lymphoid hypertrophy that is especially prominent in the mesenteric nodes but may also invade other areas of lymphoid tissue in the abdomen. This reaction as seen in the cervical and mesenteric glands may regress or go on to suppuration. Ronaldson³⁷ believes that although other areas of lymphoid tissue may suppurate during the course of scarlet fever, the appendix has a high degree of immunity to this disease.

EPIDEMIC PAROTITIS

Abdominal pain is a rare symptom of mumps. The commonly mentioned complications are orchitis, oöphoritis, pancreatitis, encephalitis and nephritis. Several cases of appendicitis complicating mumps have been reported, but the incidence is very low.

ered, 1685 cases of epidemic parotitis were admitted, 8 of which were complicated by appendicitis, an incidence of 0.47 per cent. Table 8 illustrates the time relation between the onset of parotid swelling, abdominal pain and surgical intervention. Pathological and operative findings are also included. Abdominal pain due to appendicitis occurred from the third to the tenth day after the onset of parotid swelling. In all our cases, the symptoms and physical findings were typical of appendicitis. Whereas in blood studies of uncomplicated mumps the leukocytes may be increased or occasionally decreased with a relative and often an absolute increase in lymphocytes, the cases listed here all showed a leukocytosis with increased polymorphonuclear cells. There were 6 males and 2 females, with the ages varying from five to nineteen years. In practically all the cases the appendix was either gangrenous or already perforated. These findings suggest that the appendix is especially apt to rupture during the course of mumps. In 6 of our cases, surgery was delayed for a period of twenty-four hours, and in 1 case for three days. In 1 case, appendectomy was performed on the same day that abdominal symptoms commenced, but here also an acute gangrenous appendix was found. Because of this tendency toward early gangrene and rup-

ture, it is safest to operate immediately if appendicitis is suspected in a patient with mumps.

The differential diagnosis of abdominal pain in epidemic parotitis rests between oöphoritis, orchitis, pancreatitis and appendicitis. Orchitis, which is more often unilateral than bilateral, usually occurs at the height of parotid swelling. The pain may radiate from the testis to the thighs and hypogastrium. When testicular swelling appears, the diagnosis is obvious. Pancreatitis is rarely seen before puberty. It occurs most commonly one week after parotid swelling, but may also appear before it or as late as three weeks after it. Pain and tenderness over the pancreatic regions, with at times palpable tumor, are the usual physical findings. A blood-amylase determination and elevated fasting blood sugar may clinch the diagnosis. There is difficulty in differentiating oöphoritis from appendicitis. The temperature in the former is usually much higher than in the latter and is accompanied by chills. Localization of tenderness should, of course, be of aid in the diagnosis.

Treatment in our series consisted of appendectomy as soon as the diagnosis was made. General anesthesia was administered. Convalescent mumps serum was not used in any case. There were no additional complications and no deaths.

No investigator has been able to demonstrate that any relation exists between mumps and appendicitis. The theory advanced by Benassi,⁴⁵ which is supported by Sandler and Finne,⁴¹ although without any experimental proof, holds that the virus or organism that is present in Stenson's duct migrates to the appendix by way of the blood, lymphatic system or digestive tract. The belief that the organism is present in the blood stream has some support in the known fact that orchitis or pancreatitis may be the first sign of mumps. Rosenow and Dunlap⁴⁶ in 1916 reported 8 cases of appendicitis occurring at a school where there were also 34 cases of epidemic parotitis. None of the patients had both diseases. In 4 cases, streptococci cultured from the appendix when inoculated into rabbits gave rise to parotitis. The point was raised whether the appendix and parotid gland had an affinity for the same organism. This view has fallen into disregard since Johnson and Goodpasture⁴⁷ showed that mumps is produced by a filterable virus. Wesselhoef⁴⁸ does not believe that appendicitis is due directly to the virus invasion. Because of the low incidence, Sneiderman⁴⁹ believes that appendicitis is probably a coincidental complication.

The fact that the majority of cases of appendicitis fall between the fourth and seventh days

of the contagious disease is highly suggestive of some casual relation between the two.

PERTUSSIS

Among 3064 patients with pertussis, 3 developed acute appendicitis, an incidence of 0.09 per cent. Bullova et al.⁴ reported no cases of appendicitis complicating 1219 patients admitted to this hospital in the five years before our study. Cowie¹⁰ reported 1 case of acute gangrenous appendicitis, occurring in the sixth week.

Our patients were 1 girl, aged six, and 2 boys, aged eight and nine. All cases occurred during the fourth week of the paroxysmal stage. One case was allowed to go on to perforation because the patient was thought to have bronchopneumonia with mesenteric adenitis. The leukocyte counts were, respectively, 15,300 with 73 per cent polymorphonuclear leukocytes; 15,400, with 86 per cent polymorphonuclear leukocytes; and 15,850, with 81 per cent polymorphonuclear leukocytes.

Since the temperature as a rule is elevated only at the onset of pertussis, a rise during the course of the disease has practically the same significance in detecting a complicating appendicitis as it would in a person not suffering from pertussis.

In regard to the leukocyte counts, it has been shown that during the catarrhal stage of pertussis the blood is approximately normal. This is followed by an abrupt leukocytosis with lymphocytosis during the paroxysmal stage. There is a gradual decrease in the number of white cells and in the number and percentage of lymphocytes, with diminution of the clinical signs. The majority of authors seem to think that complicating pyogenic infections do not change the already established pertussis blood picture.⁵⁰ Our 3 cases occurred late in the course of the disease, and this may explain the increase in neutrophils.

RUBELLA

There was 1 case of appendicitis among 816 cases of rubella. This occurred in a ten-year-old boy who developed abdominal pain, nausea and vomiting simultaneously with a rash. The temperature was 102°F. The leukocyte count was 7290, with 80 per cent neutrophils. The post-operative diagnosis was acute suppurative appendicitis.

The blood picture in uncomplicated rubella may be similar to that in measles. Hynes⁵¹ did serial leukocyte counts on 61 patients with rubella. There was an initial leukopenia, with the white-cell count rising to normal by the tenth day. Half the patients had absolute neutropenia until after the tenth day. One third had neutrophilic leukocytosis.

SUMMARY

The records of 29,802 cases of the common contagious diseases were reviewed for the concomitant presence of acute appendicitis, which occurred in 53 cases, an incidence of 0.18 per cent.

One hundred and two cases of acute appendicitis and pseudoappendicitis were analyzed for age, sex, leukocyte count and the time relation between the onset of the appendicitis and the manifestation of the contagious disease.

More than half the cases of acute appendicitis were found to be already ruptured at operation.

It is pointed out that physicians often hesitate to diagnose acute appendicitis in the face of obvious signs because of the presence of a contagious disease, which in its usual course is frequently accompanied by abdominal symptoms.

A review of the literature is made, and some of the reported cases are included in this study.

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MEDICAL PROGRESS

PHYSICAL THERAPY IN SURGICAL PRACTICE*

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THE application of physical therapeutic measures in nearly every field of medicine has usually been reported as an adjunct to other forms of treatment, but at times as the sole form of therapy.¹ Surgeons particularly find that in a variety of conditions these agents are beneficial. At times specialized technics are indicated, and these are best administered by a trained technician under the direction of a physical-therapy physician. For the most part, however, established procedures useful in preoperative and postoperative care can be directed by the surgeon himself. Full information on the physical principles involved, the physiologic effects and the technical details of administration of these physical measures may be found by referring to the standard textbooks on physical medicine.²⁻⁴ Also recommended is an excellent thirty-five-page summary of the most useful measures in general practice, particularly in military hospitals, recently prepared by a group of experts⁵ under the auspices of the National Research Council and the Council on Physical Therapy. It is the aim of this paper to report some of those applications of physical medicine that at the present time are being found of value in the treatment of patients hospitalized for common surgical procedures.

PREOPERATIVE APPLICATION

Physical therapy is of value in a limited number of conditions preoperatively. Local applications of heat to areas of superficial infection are frequently utilized, although on rather empirical grounds. Recent studies^{6,7} have shown that increasing or lowering the temperature has only a transient effect on the development of experimental infections. Clinical experience, however, has indicated that hot fomentations and immobilization speed the localization of superficial sepsis and in many cases are beneficial before incision and drainage. Hot, moist compresses extending well beyond the involved area are most commonly used. These may consist in layers of woolen blanket wrung out of water at 160°F. and applied to the

skin, which has previously been coated with boric acid ointment or vaseline, the entire dressing being covered with oiled silk or rubber sheeting. Since cooling occurs in about twenty minutes, the entire dressing may be surrounded by a heat cradle to maintain an elevated temperature for more prolonged periods. Cochran⁸ has recommended that tubes carrying saline solution be inserted to keep the dressing moist.

Flaxseed poultices or melted paraffin-wax dressings may be used for more retentive heating effects, but are less easily prepared. The Kenny type of hot pack^{9,10} has been found quite effective in surgical conditions¹¹ as well as in poliomyelitis. This pack consists of all-wool blanket strips that are heated in boiling water and wrung out twice through a tightly adjusted wringer at the bedside, and quickly applied. Higher initial temperatures than otherwise are safe, since the woolen material retains little moisture after wringing, thus minimizing the danger of burning. A further advantage is that after cooling, the pack is only slightly moist and not uncomfortably cold.

Thermal agents are valuable in the immediate treatment of sprains and contusions. Cold rather than heat should be applied during the first twenty-four hours, to prevent excessive hemorrhage and exudate.¹² In some conditions the use of cold is contraindicated. Application of ice bags to the abdominal wall in the presence of peritonitis, appendicitis or bleeding peptic ulcer may be deleterious because of the possible stimulating effect on peristalsis,¹³ the impediment to diagnosis from the local anesthetic action and the possible injury to the skin that may later be the site of operation.

Therapeutic exercises are of value before some surgical procedures. Individual muscle training prior to certain types of arthroplasties and tendon transplants may facilitate greater function postoperatively. Before thoracoplasties, shoulder and upper-back exercises should be learned so that the confidence of the patient in the technician and his familiarity with the required movements will make it easier to start exercises after operation.

Abdominal exercises as described by Coulter¹⁴ have been recommended before the repair of hernias by some surgeons.

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp., Springfield, Illinois: Charles C. Thomas Company, 1942. \$5.00).

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In preparation for extensive abdominal surgery, ultraviolet irradiation in mild tonic dosages may improve the general condition of somewhat debilitated patients.¹⁵ Several daily irradiations with the production of mild erythema may also speed healing of pyogenic skin infections or acne vulgaris in the operative region.

POSTOPERATIVE APPLICATION

To secure maximum comfort for patients postoperatively, attention should be given to correct bed posture, both lying and sitting. During the period of recovery from anesthesia the optimum position must of course depend on the type of anesthesia and the site and nature of the operation. Later during convalescence backache and pains referable to muscles may be due to mechanical strain, and are preventable by applying the principles of correct posture.

If the surgical condition permits, the proper recumbent position is the same as the normal standing alignment. Tight bedcovers are uncomfortable and tend to cause foot-drop and knee-flexion contractures in patients who remain supine nearly continuously. A footboard easily remedies this difficulty. When the patient is sitting in bed, pillows should be placed to support the upper back and prevent acute angulation of the neck with compression of the thorax. Postural instruction should also include correct chair-sitting and standing alignment when that stage of convalescence is reached. A well-illustrated presentation of posture in nursing care that has recently been published elucidates these important points more fully.¹⁶

It is well known that the inactivity necessitated by some operations results in loss of muscle tone and bulk, with alterations in circulation since the normal lymphatic and venous return is dependent on muscular activity. Massage, although not capable of preventing the muscular atrophy of disuse, improves tonus. It has a more important effect on circulation, for in addition to the reflex dilatation of the capillaries obtained by light stroking, heavier motions and kneading improve the venous and lymphatic return.¹⁷

Massage also has definite effects on the central nervous system, although the pathways involved are not known. Muscular and psychologic relaxation may be produced by slow, gentle, rhythmic stroking. This sedative action of massage may be used to secure sleep without the aid of drugs, as well as for its comforting effect. Well-trained nurses are expected to have developed sufficient skill to accomplish this. In the presence of pathologic conditions such as fractures and paralyses, specially trained technicians are more effective. General massage may be used for its tonic effect,

and although not resulting in an accumulation of lactic acid and other metabolites of muscular activity, it is similar to mild exercise and may be followed by a sense of fatigue.

Since muscular atrophy occurs rapidly and extensively with inactivity,¹⁸ it should be counteracted as soon as the general condition permits by muscular contractions graded in intensity. At first the exercise may consist of muscle-setting only, then free motions increasing in difficulty or in frequency of repetition. This exercise, in addition to maintaining and improving muscular strength, thus shortening convalescence, is also thought to be of value in preventing thrombophlebitis. Krebs¹⁹ has recently advocated the use of a recumbent bicycle apparatus attached to the bed to lessen the occurrence of this familiar postoperative complication.

Another complication of bed rest in elderly patients and those with some degree of arthritis is the development of painful contracted shoulders. A simple precautionary measure is to instruct or aid the patient to abduct the arm fully and rotate it externally several times daily. In the presence of pain, local heat from a luminous heat lamp or hot packs applied for twenty minutes preceding the exercises may be of benefit.

SPECIAL APPLICATION

The measures already described are of general usefulness. In addition, there are procedures that may be indicated in relation to surgery of particular regions of the body.

Abdominal Surgery

The treatment of distention, ileus and peritonitis is not within the scope of this report. Some form of local heat is frequently recommended, however, and for this purpose a simple heat cradle or "baker" containing incandescent electric-light bulbs is effective and avoids abdominal pressure.

To reduce the inflammatory reaction and edema of the stoma following a Mikulicz type of colonic resection, Welch and Krusen²⁰ devised a special applicator for internal heating. This consists of a two-way rubber tube, which is inserted in the colon and through which a current of hot water is circulated at known temperature and pressure as regulated by the Elliott-treatment machine. These authors have found that a few such treatments allow earlier progression to the second stage of the operation.

Genitourinary Surgery

Measures designed to produce hyperemia are frequently recommended as adjuncts to other forms of treatment of pelvic inflammatory disease.

Agents employing conductive heating through the abdominal wall, such as hot-water bottles, may give some temporary relief of pain, but the intra-abdominal temperature is not altered. For deeper heating and more lasting effect, short-wave diathermy may be applied to the abdominal wall.²¹ The maximum heating effect is obtained by the use of vaginal electrodes with short-wave or preferably long-wave diathermy machines.²² Similar devices for intrapelvic heating include Elliott treatments with circulated hot water,²³ methods using hot air²⁴ and, more recently, a small incandescent bulb of appropriate shape with filament temperatures that can be regulated as desired.²⁵ Hyperemia may also be accomplished through iontophoresis with acetyl-beta-methylcholine, and successful reduction of inflammation has been reported by several authors using this method.^{26, 27} Since these treatments are nonspecific, it is obvious that the simplest and safest available method that gives relief should be used.

Orthopedic and Traumatic Surgery

Physical therapy is indicated to speed restoration of motion postoperatively in the majority of patients who require bone and joint surgery. In the treatment of fractures and of traumatized skin, muscles, tendons and nerves, physical measures also play an important role. In these cases a combination of agents is most effective. Heat is required for its beneficial effect on the circulation and to relieve spasm of muscles. This is generally followed by massage of a specific type, depending on its intended purpose. At times only gentle stroking is used for reflex circulatory effect; later, deep motions are employed for mechanical relief of excessive exudate, and in some types of cases friction is used to loosen contractures. If there is spasticity of muscles, as in spinal-cord or cerebral injuries, the massage must be of a sedative type, with avoidance of stimulation of the hyperactive reflexes.²⁸ Active therapeutic exercises generally follow the primary passive procedures. These must usually be carefully supervised at first, to teach patients the correct use of weak muscles and to avoid substitution of strong muscles for weaker ones. The amount of exercise is also carefully adjusted to strength and progress. In an occasional case when relatively prolonged immobilization is required, the muscular atrophy may be successfully combated by stimulation with faradic or sinusoidal currents.²⁹

For optimum results from physical therapy for diseased or traumatized tissues, it is important that a well-trained technician administer the treatment, under supervision by a physician who understands the principles and technics involved. Detailed discussion of the methods of physical medicine as

required in traumatic surgery is so specialized, however, that it must be made the subject of a separate report.

Hand Surgery

Speedy recovery from diseases or injuries of the hand is of such importance during this period of manpower shortage that the role of physical medicine in the treatment of hands should be familiar to all surgeons called on to treat these cases. It is particularly necessary that a physical-therapy or occupational-therapy technician be given specific instructions concerning the pathologic condition present, the purpose of the treatment, what results are to be expected and the exact measures to be used. There is no place for orders such as "baking, massage and exercises." If the surgeon himself is not familiar enough with physical medicine to write an intelligent prescription, he should refer the case to a physician specializing in this work to obtain optimum results.

In the treatment of superficial injuries such as abrasions, burns and infections, rest is one of the best therapeutic agents. Correct splinting is of great importance to prevent as much as possible the interference with function of muscles and joints that always results from immobilization. Marble³⁰ has emphasized this point and has indicated the correct position for splinting various injuries to the hand. In the case of infection, heat in the form of a large fomentation is probably of benefit, and such an application acts also as a form of immobilization. Moist compresses as previously described may be used. An approved and safe electrically heated compress (the Cooley compress) has been produced by which a constant temperature can be maintained by an accurate thermoregulator. Thermometers are incorporated as an added precaution.

Since the use of chemotherapy became widespread, there has been a real danger of beginning exercises too early in these cases because of the absence of febrile reaction as a guide to the disease process. During the early mobilization period treatments should be carefully and frequently supervised by a physician, and not left entirely to the judgment of a technician or the patient himself. The arm whirlpool bath is an excellent means of supplying heat to improve circulation, and at the same time the mild massaging effect acts as an additional stimulus to the capillaries, has a sedative action on painful areas, and enables active motions, such as grasping a sponge, to be started under water. In some cases manual massage may be helpful when edema is prominent. Gentle stroking motions only are to be used. Later in cases of beginning contracture from scar tissue,

the deeper friction type of massage is indicated. Since the hand is such a complicated mechanical structure, exercises intended to improve function should almost always be active, and in many cases are best executed in the form of functional occupational therapy. Work requiring graded amounts of joint motion, muscle strength and skill may be prescribed. In addition to the improvement of hand function thus obtained, the patient himself is benefited psychologically.

Physical therapy for burn contractures should usually be begun only after surface healing is complete, particularly if there have been skin grafts.³¹ Gentle active exercises may be begun in a warm (104 to 106°F.) whirlpool bath. This is followed by massage, chiefly at the junction of normal and involved skin, to loosen contractures. Later, when there is firm scar tissue, melted paraffin wax baths for twenty minutes may precede the massage. In all cases active graded exercises and instruction in use of the hand follow the passive procedures. Tension splinting may be required in some cases, but the apparatus should be removed once or twice daily for treatment to prevent joint stiffness and loosen scar tissue. In these cases it must be recognized that no amount of physical therapy will make up for an absence of normal tissue, and treatments should be discontinued when the maximum benefit has been secured.

In the presence of nerve injury, physical therapy aims to prevent excessive muscular atrophy and to speed the regeneration of muscular contractions when the nerve has regenerated. Mild heat, gentle passive motions and electrical stimulation of muscles have been found to be of value for this purpose.²⁸

In the aftercare of sutured tendons, Mason³² has shown that gentle limited active motion may be begun in a splint at the end of the second week with safety and benefit. After four weeks, free active motion is safe, but strenuous activity should not be permitted before the end of six weeks.

It is generally believed that physical therapy will not prevent or cure Dupuytren's contracture.³³ After surgical excision of the palmar fascia, however, certain procedures are of definite value. Motion should not be allowed until the skin wound or graft site is healed, or for about two weeks. Radiant heat may be applied during this period, but no more than mild finger exercises. Later on, splintage in some cases with mild tension in extension, together with daily physical therapy, is recommended. The whirlpool bath is excellent for this purpose and is followed by graded active exercises. In my experience physical therapy may be continued for months with benefit, as evidenced by increasing function. Some patients develop

marked swelling of the phalangeal joints with tenderness and limited motion postoperatively, which persists as long as nine or ten months and clinically resembles rheumatoid arthritis in appearance. The etiologic factor is not clear. Since Dupuytren's contractures are commonly found in patients with rheumatoid arthritis of the hands, there may be an etiologic relation, the trauma of operation precipitating the arthritis. Another possibility is ischemia from prolonged use of a tourniquet during operation.

Crushing injuries to the dorsum of the hand by direct blows or pressure from clothes wringers may be extremely disabling if not treated properly.³⁴ The skin is usually not greatly injured primarily, but if excessive subfascial hemorrhage and exudate are allowed to develop, the skin may later become necrotic and will have to be replaced by grafts. The immediate application of pressure dressing, with elevation maintained for several days or longer, has been found effective in preventing this skin necrosis. Mobilization is begun when the tendency to hemorrhage and edema formation has been overcome. The whirlpool bath is employed and is followed by supervised active exercises, with great caution in allowing free active use, since only moderate exertion, particularly in activities such as wringing clothes by hand, may precipitate fresh hemorrhage.

Much has been written concerning Volkmann's ischemic contracture. As function may be greatly diminished in spite of all physical therapeutic efforts, prevention and immediate relief seem the only satisfactory methods of overcoming this condition.³⁵ The physical-therapy procedures of value have been described in detail by Meyerding and Krusen.³⁶ They consist in traction splinting, heat, massage, manipulation, exercises and occupational therapy.

Thoracic Surgery

Prevention and correction of scoliosis are problems complicating open drainage for pulmonary abscess and after thoracoplasty. The preoperative use of exercises has already been recommended. Bisgard³⁷ in his studies of the development of scoliosis in these cases has advised postural wedging. The patient lies on the affected side over a rolled pillow so placed as to act as a fulcrum, correcting the tendency to lateral deviation. In the postoperative care of thoracoplasties, sandbags may be used to further collapse.³⁸ Postural motions are indicated as soon as the local and general conditions permit, to develop muscular control, thus overcoming the tendency to shoulder-joint limitation and spinal deviation. These exercises are gradually increased in intensity and continued until the patient can stand and walk with

no deformity. The precaution of regulating the exercises should always be taken so that dyspnea and a rapid pulse rate are avoided.

When convalescence is complicated by draining sinuses, healing is occasionally speeded by local ultraviolet irradiation. For this purpose special quartz-rod applicators are available for use on the water-cooled or the newest type of air-cooled mercury-arc lamps and the so-called "cold quartz lamps."

OCCUPATIONAL THERAPY

A number of patients require a long period of convalescence following operation, and special additional measures may be helpful in rehabilitation. Diversional or recreational activity supervised by a well-trained occupational therapist may be of value in obtaining emotional control and a proper mental outlook.

Functional occupational therapy that aims at the restoration of a particular joint motion or of muscular strength and skill is of much wider usefulness than the above. This is particularly true in treating industrial or war injuries, for recovery means, in addition to primary wound healing, the optimum return of function so that former activities can be continued whenever possible. Occupational therapy can frequently be combined with physical therapy with synergistic effect. For proper correlation of treatments these two forms of therapy function best when under the direction of a physician specializing in this type of work.³⁰

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29171

PRESENTATION OF CASE

A sixty-year-old married grocer entered the hospital because of a painful mass in the upper abdomen.

The patient had been in good health until five weeks prior to admission when he fell and struck his left side against the sharp edge of a box. He had no immediate pain but several days later developed a severe "toothachy" pain just under the left costal margin near the midline and felt an extremely tender "lump" in that area. After several osteopathic treatments the pain and tenderness were relieved but the mass persisted. Approximately four weeks before admission he began to suffer with a dull, dragging, nonradiating pain in the epigastrium that usually occurred every day and generally lasted one-half to two hours. This was unassociated with meals or any food indiscretion but was aggravated by lifting. Later the pain spread over the upper abdomen and to the right upper quadrant, where it became localized. Three weeks before admission he had two episodes of acute indigestion characterized by gripping abdominal cramps and nausea and on one occasion he vomited. Ten days before admission his physician prescribed Schlesinger's solution (scopolamine, morphine and Dionin) for the pain but this seemed to aggravate the symptoms. Prior to admission he developed constipation; the occasional stool was meager and yellow. The patient had lost 15 pounds in the period of illness. There was no history of diarrhea, jaundice, general malaise or tarry or bloody stools.

The family and past histories were noncontributory. The patient had been married thirty-one years, but there had been no children.

Physical examination disclosed a well-developed and fairly well-nourished pale man who appeared chronically ill. The chest was slightly hyperresonant. There were showers of fine crackling rales at the end of inspiration over the entire posterior chest, which seemed to disappear after coughing. The heart was normal. The upper abdomen was filled with an extremely firm, resistant mass with a well-defined nodular edge

that descended with respirations. The palpable nodules varied considerably in size up to approximately 3 cm. One area of the mass, just above the umbilicus, was tender.

The blood pressure was 150 systolic, 80 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red cell count of 4,600,000 with a hemoglobin of 13.8 gm. The urine was acid in reaction and had a specific gravity of 1.018, and the sediment contained 15 white cells and many bacteria per high-power field. The blood Hinton test was positive on two occasions, and one Wassermann test was positive.

A barium meal showed "curling" in the lower third of the esophagus. There was evidence of extrinsic pressure on the anterior surface and the lesser curvature of the body of the stomach. The spleen appeared to be at the upper limit of normal. At the end of six hours the barium was in the terminal ileum and proximal colon. A barium enema revealed an annular irregular defect in the midsigmoid that was 7 cm. in length. Because of partial obstruction at this point the colon could not be completely examined. On account of the positive Hinton test the patient was treated with potassium iodide and bismuth, but without effect on the upper abdominal mass.

The patient was discharged unimproved a week after admission.

He led a semi-invalid existence but was able to get about satisfactorily. Two and a half months later his abdomen began to swell and later his ankles became swollen. Jaundice developed and he felt extremely weak. He seemed to have a great deal of respiratory difficulty, and finally died approximately three months after the hospital admission.

DIFFERENTIAL DIAGNOSIS

DR. J. H. MEANS: We had better get all we can from Dr. Holmes first.

DR. GEORGE W. HOLMES: This first film shows the mass in the right upper abdomen. It fills the whole upper abdomen and through it you can see the shadows of the kidneys, which are normal so far as size and shape go. There is no evidence that the spleen is enlarged. I cannot see it. The diaphragm is rather high on the right. My bet would be that the mass is an enlarged liver. There is some delay in the barium as it goes from the esophagus to the stomach and one might say that the patient has a small hiatus hernia. I do not see any evidence of varices.

DR. MEANS: Is it fair for me to ask whether an enlarged liver would exert extrinsic pressure

on the esophagus and cause such a picture as that?

DR HOLMES: I do not think it would. In any old person you could get a picture like this

The displacement of the stomach is shown in this film, and the mass still looks like a large liver

DR. MEANS: There is nothing wrong with the gastrointestinal tract down as far as the small bowel except that the stomach is squeezed in the front by this big mass.

DR HOLMES: There is narrowing of the colon at a point that is hidden in this view by a loop of bowel, but on turning the patient in the lateral position it can be seen. In the ordinary position it is hidden by the rectum and lower sigmoid. In this plate, taken after evacuation, there does not seem to be any great amount of obstruction to the passage of the barium into the colon. The report says there was obstruction

DR. MEANS: There is nothing wrong with the sigmoid?

DR HOLMES: The spot films were taken to demonstrate the details in this constricted area

DR. MEANS: Did you ever see such narrowing as this as a result of an inflammatory process that went with diverticulosis?

DR. HOLMES: Yes; it could be that. There is nothing very characteristic about this narrowing. It could be due to either neoplasm or an inflammatory lesion. I should like to be able to say whether it is intrinsic or extrinsic, but I am not certain about that.

DR. MEANS: It may not be intrinsic?

DR. HOLMES: No.

DR. MEANS: It may be external pressure on the bowel?

DR HOLMES: Yes; but I think it is an intrinsic lesion that has not destroyed the mucosa to the extent that one would expect a neoplasm to do. In addition, it covers a larger area than a neoplasm ordinarily does. I think I should favor an inflammatory rather than a neoplastic process

DR. MEANS: No chest plate was taken?

DR. HOLMES: We have some films that cover the lower part of the chest

DR. MEANS: You do not see any metastatic lesions?

DR. HOLMES: No

DR. MEANS: Is there anything wrong with the bones?

DR. HOLMES: No. I wish I could go farther on this film. There is one part of this area where I can see a fingerprint-like shadow that does look like tumor.

DR. MEANS: Where is it?

DR HOLMES: In the sigmoid. Here is another set of films covering the same area in which I do not see it; the mucosa is fairly normal

DR. MEANS: I think that the differential diagnosis here can be approached best by trying to solve the following questions: What is the hepatic lesion? What is the colonic lesion? Are they related one to the other? and, Have they anything to do with the positive Hinton test? If there is doubt about the nature of the lesion in the sigmoid and if it were my case I should want to have a sigmoidoscopy done. It seems queer that it was not done

DR. TRACY B. MALLORY: The lesion was thought to be too high for that

DR. MEANS: Is it too high to reach with a sigmoidoscope?

DR. HOLMES: I should think so

DR. MEANS: Still, there might have been lesions lower down than they could have picked up. I think the examination was indicated. I should like to know more about the chest because of the rales and I am interested in whether there were any metastases in the chest. Dr. Holmes says there were none in the bones—at least in the ones he saw.

First of all, I think it is fair to assume that this large mass in the upper abdomen was the liver. What else could it have been? It was not spleen because we have been told that the spleen was not enlarged. It was not kidney, since we have also been told that the kidneys were not enlarged. I do not see how it could have been pancreas. It does not sound like any pancreatic lesion that I know of. It had an edge, and the only organs that have an edge are spleen and liver. Also it moved down with respiration. It seems to me that there is no doubt that the mass was a big liver; in addition, the edge was very nodular, having nodules up to 3 cm. in diameter, which were hard. The relation of the injury to this we might take up. It is not at all uncommon for a person to have a large mass of some sort in the abdomen about which he knows nothing, it produces no constitutional symptoms and is first discovered after he has injured it. I think in this case the patient may have bruised this mass and have had a hematoma or something of that sort in it. The story as we get it is that he had symptoms of some difficulty on bending over, which were aggravated by lifting. The symptoms that go with a large abdominal mass may be related to posture. The complaint is made that it is painful to bend over; sometimes position makes a definite change in the pain.

I am interested in the constipation. It says that this occurred "prior to admission." Of course we

should like to know how long ago. Whenever anyone in old age develops progressive constipation one thinks at once of the possibility of a malignant lesion in the colon, and this x-ray picture could, of course, represent a malignant lesion in the colon.

We then come to the positive Hinton test. The patient must have had syphilis at some time in the past. Could the lesion in the liver have been syphilitic? He had positive Hinton and Wassermann tests, which is of great importance. We know that they gave him some antisyphilitic treatment, which is said to have been without effect on the upper abdominal mass. I should like to know how vigorously this treatment was pushed.

DR. EARLE M. CHAPMAN: The patient was in the hospital a week. On the last day he received bismuth and, a few days before, potassium iodide. This treatment was continued when he went home. The mass became smaller over the first three or four weeks of treatment, and the patient felt better.

DR. MEANS: Now we are in a dilemma. However, I think the man had one of two things. A liver with lumps in it as big as these are said to have been can only be explainable by cancer or syphilis. I do not believe that a syphilitic liver would give lumps that could be felt as easily as this. There is a condition called *hepar lobatum*, in which the liver is broken into subdivisions that can be felt perhaps as nodules. The patient could have had syphilis of the liver and a lesion in the bowel that was not carcinomatous. I do not know of regional inflammation of the colon of the sort one sees in the ileum. I do not believe the lesion is tuberculous. Dr. Holmes says that this lesion might not have been intrinsic.

DR. HOLMES: I think it is.

DR. MEANS: I am going to assume it is, because I should be in a worse hole if it was not. It might have been due to chronic diverticulosis. If that were the case, I do not see why the patient did not have a past history of colonic symptoms, which apparently he did not have, beyond a little constipation.

I think I shall wind this up by saying, first, that the patient had cancer of the sigmoid, which had metastasized extensively to the liver. I believe he had syphilis, but the syphilis did not play a part in the symptomatology. On the other hand the fact that he got better on antisyphilitic treatment is disconcerting and makes one wonder if it could have been a syphilitic liver. If it was a syphilitic liver I do not see why he did not keep on getting better on antisyphilitic treatment. I suppose he could have had cancer in the bowel and syphilis in the liver, but that is most unlikely.

But I am going to admit that the liver could have been syphilitic and that the lesion in the colon could have been a benign one.

DR. MALLORY: I should like to ask Dr. Holmes a question. Could the lesion in the sigmoid be lymphogranuloma venereum?

DR. HOLMES: Yes; I think that is possible.

DR. MALLORY: Lymphogranuloma could give local involvement of the colon and might, of course, be associated with syphilis.

CLINICAL DIAGNOSES

Hepar lobatum.

Syphilis.

Carcinoma of sigmoid, with massive metastases?

DR. MEANS'S DIAGNOSES

Carcinoma of sigmoid, with metastases to liver.

Latent syphilis.

ANATOMICAL DIAGNOSES

Carcinoma of sigmoid, with metastases to regional nodes and liver.

Arteriosclerosis, aortic, severe.

Icterus.

Ascites.

Pulmonary tuberculosis, healed, apical.

Serologic syphilis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed that the patient did have a cancer of the sigmoid; the liver weighed 5000 gm. and was almost completely replaced by metastatic tumor. There was no evidence of syphilis that we could discover at the autopsy. The lungs showed healed apical tuberculosis but no metastases.

DR. CHAPMAN: Our reasoning was very much the same as that of Dr. Means in approaching this problem. We thought that it was probably cancer but that the patient's only hope was for us to act as if it was related to syphilis. For that reason Dr. Francis R. Dieuaide saw him and raised an instructive point. Here was a man of sixty who was suddenly discovered to have positive serologic tests for syphilis. After much pressure we obtained from him a story that he had acquired a primary lesion five years before coming to the hospital. He had had no specific treatment. This represented untreated syphilis of five years' duration and Dr. Dieuaide pointed out that this was just about the right interval for the appearance of a gummatous lesion, a *hepar lobatum* in the liver. So we treated him on that basis. The intestinal lesion was too high to view with a sigmoidoscope, and we did not try it. The improvement following the first

four injections of bismuth was striking. The patient felt better and went back to work. The lumpy mass definitely decreased in size and was less tender. After he had had six or seven injections of bismuth, the nodules began to increase, the pain returned and he went into a progressive downhill course.

DR. MEANS: Did you find any evidence of trauma in the liver that might have been the result of accident—hematoma or anything of that sort? Have you any explanation for the diminution in size after the antisiphilic treatment?

DR. MALLORY: No; we could find no evidence of syphilis. Regarding the improvement, I am reminded of the old story attributed to Dr. Osler. The question was, "What could put 50 pounds on a man with cancer of the stomach?" And the answer was, "An optimistic consultant."

CASE 29172

PRESENTATION OF CASE

First admission. A twenty-one-year-old housewife was sent to the hospital because of a rash that first appeared on the face but that more recently had spread to the arms, legs and oral mucous membranes.

At the age of nine years following a severe sunburn, the patient developed scarlet, slightly raised areas of skin eruption over the cheeks and bridge of the nose that did not itch or burn. Two months later similar small areas of eruption developed on the chin and the left forehead. Behind the ear there was a 1-cm. area of alopecia. Follicular plugging and gaping of the sweat pores was evident on the upper lip. Some of the older lesions on the chin became scaly and scarred but the lesions remained rather constant until two years before admission, when they almost completely cleared after treatment with aluminum acetate and sodium bicarbonate compresses. However, two small areas on the chin persisted as pigmented spots.

Approximately two months before entry, one month after becoming pregnant, scaling "blotches" appeared on the face without any associated pain, itching or burning, and the patient noted raised, very sore nodular areas on the roof of the mouth that felt like "blisters." At about this time she noticed slight swelling at the base of the fingernails of the left third and fourth fingers associated with local pain and burning. The skin at these points was smooth and shiny. Soon the entire fingertips became red, hard and scaly and small pink spots appeared on the hands. These later increased in size to 1.5 cm. and developed

scarlet centers, and scaling brown rings about them. Occasionally these areas burned and itched, and sometimes they were painful. Three weeks before admission similar changes developed on the extensor surfaces of the arms, feet and lower legs. She had recently suffered with occasional mild attacks of occipital headache, which lasted two or three days. During the two days prior to admission her hands and feet seemed swollen.

The patient's mother suffered with syphilitic aortitis. As a child the patient had measles, mumps, scarlet fever, chicken pox and whooping cough without sequelae. There was no history of rheumatic fever.

Physical examination revealed a young woman who did not appear to have any discomfort. There were irregular "blotchy" groups of lesions on the face that were more marked on the cheeks and chin than on the forehead. The lesions were irregularly shaped, purple-red in color, slightly raised and moderately rough. There was a fine scaling of the skin at the tip of the nose. There were a few indurated brownish round "spots" on the chin and at the corners of the mouth and on the arms, hands, legs and feet. Many lesions were round, approximately 2 to 4 cm. in diameter, and had a scarlet scaly center and a brownish ring about the periphery. There were a few small lesions on the chest. An indurated red swelling was present at the base of each fingernail. There was marked redness of the tips of the left second, third and fourth fingers with cracking and scaling of the skin. The upper palate was red and covered with small blisters. Scattered coarse rales were audible posteriorly at the apex of the right lung, and there was a soft systolic murmur in the left parasternal area.

The blood pressure was 130 systolic, 74 diastolic. The temperature was 98.6°F., the pulse 83, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,610,000, with a hemoglobin of 85 per cent, and a white-cell count of 4600 with 66 per cent neutrophils, 26 per cent lymphocytes, 5 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. The urine was normal. The Hinton test was negative. A Friedman rabbit test indicated pregnancy.

In the x-ray film of the chest the lung fields and costophrenic angles were clear. The diaphragm was normal in position. There appeared to be rather indefinite enlargement of both hilar regions. The heart shadow was normal in size and shape. A gastrointestinal series and Graham test were negative. X-ray films of the sinuses showed a large polyp in one of the antrums along the medial wall and small polyps along the

floor of the antrum. The ethmoid sinuses showed no abnormality. Biopsies of the skin of the leg and arm were consistent with lupus erythematosus. The patient was treated with topical compresses and discharged two weeks later only slightly improved.

Second admission (one month later). The patient was readmitted because of a red, tender, painful swelling of the right ankle that appeared a day after leaving the hospital and gradually resulted in stiffness of the joint. The eruptions on the hands had cleared slightly, but those on the legs and feet were somewhat worse. The lesions elsewhere were unchanged. Dermatographia of the trunk was striking. There was a tender, warm, reddish swelling of the right ankle, where several of the skin lesions appeared to be secondarily infected. The fundus of the uterus was felt four fingerbreadths above the symphysis pubis.

The temperature was 100°F., the pulse 93, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,070,000, with a hemoglobin of 80 per cent, and a white-cell count of 3900, with 58 per cent neutrophils, 36 per cent lymphocytes and 6 per cent monocytes.

Two days after admission, soreness and stiffness developed in the elbows, the shoulders and the right knee and ankle, and the right knee was slightly swollen along the medial aspect of the patella. The swelling of the right ankle had improved following treatment with compresses of 1 per cent chlorinated soda. Oil of wintergreen applied topically made the painful joints more comfortable, but two and a half weeks later, swelling and stiffness spread to the joints of the hand and the left elbow. An infected excoriation developed on the right buttock, and following an extension of the pustular lesions on the right foot, tender, fluctuant adenopathy developed in the right groin associated with pain, tenderness and rigidity in the right lower quadrant that necessitated open drainage. Because beta-hemolytic streptococci were cultured from the pus and a few petechiae occurred beneath the beds of the fingernails the patient was started on orally administered Prontylin (10 gr., three times a day). The temperature, which had been spiking to 102.5°F. each day, became normal and the patient seemed markedly improved. Forty-four days later, after having received 795 gr. of Prontylin, she complained of headaches and severe dizziness, which disappeared when the drug was withdrawn and promptly returned when it was used again after a rest period of three days. Approximately three weeks later, because the right groin wound continued to show

a positive culture for beta-hemolytic streptococci, the patient was started on daily doses of 10 cc. of Prontosil intramuscularly; after three days the initial dosage of Prontylin was again tried but this was discontinued after six days of persistent vomiting. The patient continued unchanged, and six and a half months after admission, because of the onset of labor, she was transferred to a lying-in hospital for delivery.

Third admission (ten days later). The patient was readmitted because of continued suppuration in the right groin. Labor had proceeded uneventfully under Pentobarbital and scopolamine analgesia, with drop ether anesthesia at the time of delivery, and the patient was delivered twenty-three hours later. The fetal heart remained good until two hours before delivery but then was lost. At birth, the stillborn infant was covered with bright golden-yellow vernix caseosa. Post-mortem examination showed this material in the bronchi, trachea and stomach, and petechial hemorrhages in the epicardium and pleura. On the third day after delivery, the mother's temperature was 102.6°F. and she continued to run a low-grade evening fever to the day of discharge.

On admission the temperature was 101°F., the pulse 100, and the respirations 20.

The red-cell count was 4,000,000, with a hemoglobin of 65 per cent, and the white-cell count 17,450, with 66 per cent neutrophils, 22 per cent lymphocytes and 12 per cent monocytes.

Many of the skin lesions seemed scarred and pigmented. The infection in the right groin was treated with compresses and gradually improved. The patient was discharged a month later somewhat improved.

Fourth admission (five and a half years later). The patient, then twenty-seven years old, was readmitted because of extreme fatigue and chills and fever. Two and a half years before re-entry she began to have vague muscular pains in the chest, neck, back, arms and hands, particularly associated with movement, and these gradually became quite severe. However, there was no apparent associated joint pain. One and a half years before re-entry, after having five teeth extracted, a chin lesion, the site of mild activity, cleared up and she felt quite well. Three weeks before re-entry she began to feel exhausted after only mild daily exertion. Frontal headaches that radiated to the occipital region developed and became progressively worse. However, acetylsalicylic acid always provided some relief. Two weeks before re-entry, she had a "stiff neck" with an area of soreness on the right side below the hairline, from which pain radiated to the right shoulder when she turned her head to the left. This was partially

ieved by acetylsalicylic acid ointment. Three days before re-entry she had a nosebleed after wiping her nose. That night she was awakened by a shaking chill and found that her temperature was 102°F. After a drenching sweat the temperature became normal. Approximately eighteen hours later, she had "chilly sensations" running and down her spine, which were partly relieved by acetylsalicylic acid. She awakened three hours later feeling warm and perspiring, and all the muscles seemed to ache. During the two weeks prior to admission she had lost 12 pounds.

Recently, the patient had noticed evening ankle edema after she had been on her feet all day. During the past year she recalled having twice passed blood clots "as big as a fist" during a menstrual period.

On examination, the patient appeared tired and anemic. She complained of a frontal headache and pain in the neck and shoulder. The skin lesions were scarlet and pigmented. There were small, fairly firm, tender, movable lymph nodes in the posterior cervical triangles. The heart, lungs and abdomen were normal. All tendon reflexes were sluggish, especially at the knees and ankles. The blood pressure was 184 systolic, 108 diastolic. The temperature was 101.4°F., the pulse 60, and the respirations 21.

The red-cell count was 4,560,000, with a hemoglobin of 10.9 gm. per 100 cc., and the white-cell count 5000, with 74 per cent neutrophils, 20 per cent lymphocytes, 2 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils. The urine was alkaline in reaction, had a specific gravity of 1.014, and showed a +++ test for albumin and a +++ Sulkowitch test for urinary calcium; the sediment contained 2 white cells per high-power field. When checked four days later, the urine was acid in reaction and contained no albumin. A phenolsulfonephthalein test showed 35, 20 and 10 per cent excretion of the dye in fifteen, thirty and ninety minutes respectively.

The patient gradually improved on symptomatic treatment and was discharged one week later.

Final admission (twelve days later). The patient was followed in the Out Patient Department, where she complained only of headaches that were relieved by acetylsalicylic acid. She was brought to the accident room in coma. Because it was feared she had taken a massive overdose of barbiturate sedative, oxygen was administered and icteroxin was injected intravenously. She died fifteen minutes after reaching the hospital.

DIFFERENTIAL DIAGNOSIS

DR. JACOB LERMAN: A diagnosis of lupus erythematosus was made on the first admission, and

certainly everything I have read so far is consistent with this diagnosis.

This is a long and complicated case and instead of the usual procedure of discussing the differential diagnosis, I shall accept the above diagnosis, and see if I can rule in or out any other diagnosis as the case develops.

On the first admission the only atypical feature, if it was disseminated lupus erythematosus, was the duration of the disease, starting at nine, with a fairly typical onset following sunburn, and lasting until she was twenty-seven. I had one patient who lived eight years, which is fairly long. Most of these patients die between one and six years after onset. The lesions are quite characteristic—their color, the involvement of the face, fingernails and mouth, the leukopenia and the joint pains all fit in with the diagnosis of lupus. Finally a biopsy specimen is said to have been consistent with this diagnosis.

The statement about syphilitic aortitis in the mother raises the question of congenital syphilis in the patient. There is no evidence of any bone lesion suggestive of congenital syphilis, or of eye symptoms; and the description of the rash is not that of syphilis. Finally the Hinton test was negative. I believe we can rule out congenital syphilis.

At this point in the description there is no mention of involvement of other serous surfaces, such as the pericardium, pleura and peritoneum.

On the second admission the second atypical feature appeared—the development of a red ankle. Many patients with lupus erythematosus have joint pains. It is a very frequent symptom but I do not recall having seen an acute joint of this sort. The evidence of infection of the adjacent skin might explain the acutely infected joint. Subsequently, the patient developed the arthralgia and joint stiffness that are characteristic of lupus erythematosus. Then, the complication of suppuration in the groin, from which she suffered throughout and after pregnancy, confuses the picture.

On the third admission I cannot relate the death of the fetus and the description of the vernix caseosa with the patient's condition. I asked an obstetrician what a golden-yellow vernix caseosa signified and he said that it indicated erythroblastosis foetalis. Even if this child did have erythroblastosis foetalis I do not see any connection between it and the patient's complaints. Obviously the child died of intrauterine asphyxiation, and the findings are characteristic. We may pass this off without any further comment.

The fourth admission introduces a new group of symptoms, namely, frontal headaches, which radiated to the occiput, stiff neck, nosebleed, fever,

chills, weight loss, ankle edema, and menorrhagia on several occasions. These symptoms are consistent with lupus erythematosus, particularly the nosebleeds and the menorrhagia. This bleeding tendency raises the suspicion that some of the other symptoms were due to bleeding. The headaches could have been due to intracranial bleeding. She also developed cervical adenopathy, which is common in lupus erythematosus. Another interesting finding is the elevation in blood pressure. On the first admission the blood pressure was normal. Some patients develop hypertension because lupus erythematosus is a generalized vascular disease. Many eventually develop vascular nephritis. This patient had transient albuminuria. Renal injury is characteristic of lupus erythematosus. The importance of renal injury is that when a patient develops it, the prognosis becomes poor. From that point on the patient usually goes downhill very fast. Throughout the course we find evidence of leukopenia and mild anemia.

Thus far almost everything fits in with the picture of lupus erythematosus. I have yet to find anything that would steer me away from this diagnosis except for the headaches and the pain in the back of the neck, which are a bit atypical.

Finally, she re-entered the hospital in coma. If we assume that this was disseminated lupus erythematosus, there are several possibilities to account for the coma. I think we can forget barbiturate poisoning, or at least not consider it seriously. Although picROTOXIN was given, there is not much evidence to indicate that she took a lot of barbiturate. One cause of coma in a patient with lupus erythematosus is intracranial bleeding, particularly subarachnoid bleeding. This would also explain the headaches that she developed over a period of three or four weeks. There also could have been extensive intracerebral hemorrhage without localizing signs. Another possible cause of coma is an embolus from a verrucous endocarditis, which is common in disseminated lupus erythematosus.

I should like to consider other diagnoses and see if I can rule them out. One is periarteritis nodosa. In favor of this were the vague arthralgias, the development of hypertension, the albuminuria, the nosebleeds and the headaches. The skin lesions were not those of periarteritis nodosa. Furthermore, there were no characteristic tender nodules along the course of arteries, no eosinophils, no asthma and no leukocytosis. Leukopenia was a constant finding except during one episode of infection.

One should also consider dermatomyositis. In favor of this are muscle pains, weakness, fever and edema of the face. The skin lesions are quite consistent, but are more hemorrhagic than those usually seen in dermatomyositis. On the other hand the absence of muscle induration, leukopenia and arthralgia are against this diagnosis.

I shall also mention sarcoid, although there is little in favor of it. There was no bone, lung or spleen involvement, and the rash was not that of sarcoid. In addition, there was no generalized adenopathy.

The patient could have had an independent brain tumor to account for the last episode of headaches and coma, but there is nothing in the description to lead me to this.

I am left with a diagnosis of disseminated lupus erythematosus, ending fatally with subarachnoid or intracerebral hemorrhage, although there is no mention of serous involvement. I shall predict that there was fluid in the pericardium, pleura and peritoneum.

DR. TRACY B. MALLORY: Dr. Swartz, would you like to add anything?

DR. JACOB H. SWARTZ: My comment is more or less that of a dermatologist. I should like to add that it is unusual for lupus erythematosus to begin at such an early age.

Generalized lupus erythematosus superimposed on a discoid type should be distinguished from acute and subacute lupus erythematosus. I prefer to group acute and subacute lupus erythematosus with periarteritis nodosa and dermatomyositis. Frequently they cannot be differentiated by skin lesions or other manifestations, and I therefore disagree with some of Dr. Lerman's remarks. Periarteritis nodosa and dermatomyositis may have varied accompanying skin lesions. Furthermore, acute disseminated lupus erythematosus may have no skin manifestations or very few.

In these three diseases one can find clinically a good deal in common, such as pyrexia, arthralgia, splenomegaly, renal disturbance and thrombocytopenic purpura. Oral lesions may be present in dermatomyositis although not so commonly as in acute lupus erythematosus. Sensitivity to sunlight is present in all but more so in lupus erythematosus.

CLINICAL DIAGNOSES

Lupus erythematosus disseminatus.
Nembutal poisoning?

DR. LERMAN'S DIAGNOSIS

Disseminated lupus erythematosus, with terminal subarachnoid or intracerebral hemorrhage.

ANATOMICAL DIAGNOSES

Disseminated lupus erythematosus.
Periarteritis nodosa of kidneys and pancreas.
Cerebral hemorrhage.
Bronchopneumonia, slight.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The chief gross findings were a completely adherent pericardium, a slightly hypertrophied heart and some very abnormal kidneys, which were larger than normal, with pale grayish discolorations and a few petechial hemorrhages. There was just a trace of bronchopneumonia. The immediate cause of death turned out to be a large cerebral hemorrhage, which had completely destroyed the left internal capsule and filled the left lateral ventricle and the third and fourth ventricles. Approximately 50 cc. of blood was evacuated. Microscopic examination provided surprise in that the kidneys showed very characteristic and extensive lesions of periarteritis nodosa, and similar vascular changes were also seen in the pancreas but were not picked up in any other organs. The spleen was slightly enlarged, weighing 170 gm., and the splenic arterioles showed marked periarteriolar fibrosis of the type described as characteristic of lupus erythematosus, but which is certainly also seen occasionally in a variety of other diseases and is not present in all cases of lupus erythematosus. The case

is reminiscent of one that the late Dr. Soma Weiss discussed here five years ago.¹ In that patient there was an initial onset of apparently characteristic thrombocytopenic purpura temporarily cured by splenectomy, but followed later by a characteristic clinical picture of acute disseminated lesions. That case at autopsy likewise showed typical anatomic lesions of periarteritis nodosa in the kidney, such as this one did.

We unfortunately have no histologic examination of the brain and so we cannot state whether the hemorrhage was due to local vascular lesions in the brain or to the purpuric tendency that is so characteristic of these patients. One is left with the question whether to make a diagnosis on the clinical syndrome, which would certainly be lupus erythematosus, or one based on histologic lesions, which would have to be periarteritis nodosa. In recent years the trend of opinion has been to regard periarteritis nodosa as a nonspecific vascular reaction that occurs in the course of a variety of diseases and has been reported in association with serum sickness, bronchial asthma, trichinosis and a variety of other conditions. My own preference for the primary diagnosis on this case is lupus erythematosus.

REFERENCES

- 1 Case records of the Massachusetts General Hospital (Case 24201) *New Eng J Med* 218 838 843, 1938
- 2 Rich A. R., and Gregory, J. E. Experimental demonstration that periarteritis nodosa is manifestation of hypersensitivity *Bull Johns Hopkins Hosp* 72 65 88, 1943

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

MEDICAL OFFICERS FOR THE ARMED FORCES

AN EDITORIAL in the March 27 issue of the *Journal of the American Medical Association* states that the armed forces in 1943 will require six thousand physicians over and above those obtained from recent graduates, interns and residents and that the responsibility for supplying these medical officers rests largely, if not entirely, on the young physicians in the large cities of the country, particularly those of the eastern seaboard, including Boston. Furthermore, it is suggested that, if physicians who have been declared available by the Procurement and Assignment Service do not volunteer, the state medical journals publish lists

containing the names of such men, as well as those of the men who are already in active service—an unpleasant and—one hopes—unnecessary threat that smacks a bit of the lack of one of the “freedoms” for which the United Nations are fighting.

Certainly no one should question the needs of the combat services for medical officers, even though some may wonder why the tables of organization of the United States Army and Navy call for greater numbers per fighting unit than do those of the Canadian and British forces, especially when the health of the civilian population, which has been called on to produce fantastic amounts of supplies and equipment, is of basic importance. On the other hand, until regulations more drastic than those now in existence are promulgated by the Selective Service System, most physicians, because of dependents, cannot be *made* to enter military service. The question whether a man is essential or available is often difficult to decide, and certainly some of the physicians who have been declared available have valid reasons for not volunteering. This, however, does not excuse the majority; if they are needed,—and they are,—they should be willing to make the sacrifices that millions of other men have already made. Failure to do so will leave just as large a blot on one's record of self-esteem as will indictment by the “bar of public opinion.”

THE COMMISSIONER OF PUBLIC HEALTH

GOVERNOR SALTONSTALL's choice of a man to succeed Dr. Paul J. Jakmauh as commissioner of public health was well considered.

The appointee, Dr. Vlado A. Getting, of Worcester, graduated from Harvard Medical School in 1935, and subsequently received the degrees of master of public health and doctor of public health from Harvard University. He interned at the Worcester City Hospital, and later became associated with the Massachusetts Department of Public Health, first as an assistant epidemiologist, then as director of a mosquito survey and eventually as a district health officer. In 1942 he became com-

missioner of health for the City of Worcester. Since 1939 he has held the positions of research assistant and assistant in epidemiology at the Harvard Medical School and the Harvard School of Public Health.

Having been forced to resign from the Medical Corps Reserve of the United States Army in 1942 because of physical disability, Dr. Getting now faces a responsibility that is as great as any that might arise in the armed forces. What he lacks in years of experience is more than counterbalanced by an excellent basic training in practical and administrative public health matters, and the *Journal* takes this opportunity of extending to him its congratulations and of prophesying that his years of service will be marked by many advances accruing to the health of the people of the Commonwealth.

MEDICAL EPONYM

TROUSSEAU'S PHENOMENON

Professor Armand Trousseau (1801-1867) of the Medical Clinic of the Faculty of Medicine of Paris describes this sign in a lecture on tetany which is included in the second volume (page 107) of his *Clinique Médicale de L'Hotel Dieu de Paris* (Paris, 1862). A portion of the translation follows:

One may cause the attack to recur at will, even in patients who have been free from them for twenty four, thirty six, forty-eight or seventy two hours or even longer. In order to do this, it is enough, as I told you a moment ago, to exert pressure on the affected limbs whether over the course of the principal nerve trunks or over the blood vessels in such a way as to interfere with the arterial or venous circulation.

I was led by chance to discover this influence of pressure. While performing a phlebotomy from the arm on a woman who was suffering from [tetanic] contractures, I noticed that as soon as constriction was made with the tourniquet, there resulted an attack in the corresponding hand. I first thought that congestion produced by compressing the veins was the cause. However, in seeking to understand this phenomenon more clearly, I found that in other patients compression of the arteries acted in identically the same manner. Since then I have repeated the experiment many times, and inasmuch as it results in no inconvenience for the patients since the attacks cease immediately when the procedure is stopped, I have often performed it before you. Now you will have noticed that the contracture showed itself not only on interfering with the arterial or venous circulation, but also on exerting pressure either over the

median nerve in the arm or on the brachial plexus above the clavicle, and was immediately preceded by a sensation of tingling, which is the first symptom. These muscular spasms occur on compression of the femoral artery after placing a ligature about the thigh, or more simply still by firmly squeezing it between the two hands or by pressing over the sciatic nerve, although it is not so easy in the lower extremities.

This phenomenon, which is interesting in itself, is not without practical application. It may contribute something to diagnosis for in no other convulsive affection can one produce an effect of this nature by similar means.

R W B

MASSACHUSETTS MEDICAL SOCIETY

ANNUAL MEETING OF THE COUNCIL

The annual meeting of the Council will be held in the Georgian Room of the Hotel Statler, Boston, on Monday, May 24, 1943, at 7 00 p m. This meeting will be preceded by the Cotting supper which will be served in the Salle Moderne of the same hotel at 6 00 p m.

Business

- 1 Presentation of record of the stated meeting of the Council held February 3, 1943 (Published in the *New England Journal of Medicine*, issue of March 18, 1943)
- 2 Reports of standing and special committees
- 3 Election of officers and orator
- 4 Appointment of committees for ensuing year
- 5 Such other business as may lawfully come before the meeting

MICHAEL A. TIGHE, *Secretary*

The two following items are submitted for advance information to the members of the Council and of the Society:

REPORT OF COMMITTEE ON NOMINATIONS

The Committee on Nominations of the Massachusetts Medical Society met on April 14, 1943, at 8 Fenway, Boston, and selected the following list of officers for the year 1943-1944:

President Roger I. Lee, Suffolk
Vice president Daniel B. Reardon, Norfolk South
President-elect Elmer S. Bagnall, Essex North
Secretary Michael A. Tighe, Middlesex North
Treasurer Eliot Hubbard, Jr., Middlesex South
Assistant Treasurer Norman A. Welch, Norfolk
Orator Joseph C. Aub, Suffolk

NOTE FROM EXECUTIVE COMMITTEE

The Committee to Aid the Boston Medical Library, on February 3, 1943, recommended that the earnings of the Massachusetts Medical Society's Building Fund be turned over to the Boston Medical Library to make the library staff more efficient.

The Council referred this matter to the Executive Committee of the Council so that the attention and study

which it deserves may be taken by it and that its report be given at least 20 days before the annual meeting, if it is possible to do so."

In compliance with this directive, the Executive Committee hereby gives notice that it will offer the following recommendations at the annual meeting of the Council to be held on May 24, 1943:

1. That the Massachusetts Medical Society acquire the space now occupied by the *Journal of Bone and Joint Surgery*.

2. That the Massachusetts Medical Society pay to the Boston Medical Library as maintenance a sum of money, up to \$6500 per annum, for its quarters thus enlarged.

MICHAEL A. TIGHE, *Secretary*

DEATHS

KAAN—GEORGE W. KAN, M.D., of Sharon, died April 14. He was in his eighty-ninth year.

Dr. Kaan received his degree from Harvard Medical School in 1890. As one of its two founders, he was active in the work of the Boston Dispensary for Women from 1900 until his retirement from practice in 1924. He was a member of the Massachusetts Medical Society and the American Medical Association.

Two daughters, a brother and two sisters survive him.

LAURIN—THEOPHILE LAURIN, M.D., of Lowell, died April 10. He was in his seventy-third year.

Dr. Laurin graduated from the Baltimore University School of Medicine in 1895 and from the University of Bishop College Faculty of Medicine, Montreal, in 1899. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, two sons and three daughters survive him.

WAR ACTIVITIES

INDUSTRIAL HEALTH

TUBERCULOSIS IN INDUSTRY

Seventy-seven war industries in 11 states were surveyed by the eight 35-mm. photofluorographic units operating in industry prior to February 1, 1943, reports the Office of Tuberculosis Control, United States Public Health Service.

A total of 194,896 individuals were x-rayed. Tabulations on results are available for 125,190 people. Of these 1631, or 1.3 per cent, were found to have significant pulmonary tuberculosis. The distribution of the positive cases by stages of the disease was as follows: 874, or 53.6 per cent, minimal; 707, or 43.3 per cent, moderately advanced; and 50, or 3.1 per cent, far advanced.

In the District of Columbia, 28,098 government workers have been x-rayed. Exactly 300 cases of pulmonary tuberculosis have been discovered, an incidence of 1.1 per cent. Of these 182 (60.7 per cent) were minimal, 106 (58.3 per cent) moderately advanced and 12 (4.0 per cent) far advanced. In addition, 1300 workers at the National Institute of Health have been x-rayed. Among these, 15 cases of tuberculosis were found—9 minimal and 6 moderately advanced.—Reprinted from *Industrial Hygiene* (March, 1943), a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

CORRESPONDENCE

RESTORATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held April 14, the Board voted to restore the license to practice medicine in the Commonwealth of Dr. Daniel E. Nyman, 31 Chandler Street, Arlington.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held April 14, the Board voted to revoke the license of Dr. Solomon P. Bialow, 94 Adams Street, Waltham, Massachusetts, because of gross misconduct in the practice of his profession as shown by his conviction in court.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Doctors of the Mind: The story of psychiatry. By Marie Beynon Ray. 8°, cloth, 335 pp. Boston: Little, Brown and Company, 1942. \$3.00.

This is an unusual type of book. The author has combined the history of psychiatry with an insight into the latest advances. She is a journalist and writer, an associate editor of *Harper's Bazaar* and a former editor of *Vogue*. She has read widely in the history of psychiatry, and often enlivens her knowledge by taking the reader into the clinic or hospital of a famous figure of the past.

Interwoven with this is a report on the newer knowledge, such as the shock treatment for schizophrenia and the history of frontal lobectomy. Names of men currently active in the profession are frequently quoted. The book is aimed to give the reader a view of psychiatry not only of the past but also of the present.

Written in a journalistic style, there is little, in the opinion of the reviewer, that appeals to the average doctor. Literature of this type, however, has a place, for one feels that the author has conscientiously gathered her facts, even if her enthusiasms have outweighed her sense of judgment. She has dramatized a good deal that for the scientist has little drama and tends to "oversell" doctors, particularly those who work in laboratories, to the public.

Night of Flame. By Dyson Carter. 8°, cloth, 337 pp. New York: Reynal and Hitchcock, Incorporated, 1942. \$2.50.

The story is told about the drama of life within a hospital. It is a fast-moving narrative, packed with excitement and tragedy. The author has a good insight into hospital life, but like so many men writing novels of this type, he has packed into a brief space of time enough thrills to cover a hundred years of ordinary hospital life. The characters are somewhat overdrawn, and in the opinion of the reviewer, the book falls below the standard set by current similar works.

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SPINA BIFIDA AND CRANIUM BIFIDUM*

I. A Survey of Five Hundred and Forty-Six Cases

FRANK D. INGRAHAM, M.D.,† AND HENRY SWAN, M.D.‡

BOSTON

DURING the last two decades, 546 infants and children have been seen at the Children's Hospital with spina bifida or cranium bifidum. Associated with these conditions in the minds of both the laity and the medical profession is a rather deep pessimism. It seems worth while to analyze this group of patients, therefore, to see whether there can be established any reasonably definite criteria for prognosis, for operative therapy and for operative technique and whether such an attitude of hopeless pessimism should not be modified by examination of the actual end result in a large series of cases.

INCIDENCE

Race, sex and economic status seem to have little bearing on the incidence of spina bifida. All our patients were members of the white race. Females seem slightly more liable than males, 296 patients being girls and 250 boys. The incidence in the different economic levels seemed proportionate to the total number of patients on each level. The ratio of incidence to the number of new patients seen at the hospital during the last twenty years is 1:4150.

RELATION TO FAMILIAL OR ASSOCIATED ANOMALIES

The familial incidence of spina bifida is shown in Table 1. In 16 (6 per cent) of the 277 cases in which information was available, the patients admitted spina bifida in the family. Approximately an equal number admitted anomalies other than spina bifida.

The frequency with which spina bifida is associated with other congenital anomalies in the

same patient is impressive. In 232 patients, or slightly more than half the series, 570 associated anomalies were recorded. Even this large number is probably an underestimate, for two reasons.

TABLE 1. Incidence of Familial Congenital Anomalies.

FAMILY HISTORY	NO. OF CASES
Congenital anomaly denied	246
Spina bifida ..	16
Other anomalies	15
No data . . .	269
Total	546

First, in a number of the records no statement is made concerning the presence or absence of associated lesions; these are chiefly the records of patients who were seen only in the Out Patient Department (often on only one or two occasions) and extensive examination and skeletal x-ray studies were not done and in whom the presence of hernial sacs, genitourinary anomalies or skeletal defects might well have remained undetected. Secondly, many of the internal anomalies can be definitely established only by post-mortem examination, and this was done in relatively few cases.

It is with some hesitation, then, that we give Table 2, fearing that misunderstandings may arise. It must be realized that this is a mere tabulation of all the lesions noted and recorded from such diverse sources as records from the Out Patient Department and autopsy protocols. It is probably incomplete, particularly regarding internal anomalies, and to use it to demonstrate the comparative frequency of the associated anomalies is unwarranted. For example, only 20 cases of Arnold-Chiari malformation are listed. This apparently low incidence of brain-stem anomalies must be largely a factor of the method of the compilation of the data. When the Arnold-

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Chiari malformation is found, in our experience it is usually associated with the presence of a myelocoele. The patients with myelocoele, however, are usually the poor-risk patients and few come to operation, more being institutionalized or cared for at home, and thus not dying in the hospital

TABLE 2 Associated Congenital Anomalies.

ANOMALY	NO OF CASES
Hydrocephalus	208
Clubfoot	102
Bones	94
Vertebrae (including 7 cases of Klippel-Feil syndrome)	49
Ribs	23
Skull	16
Sprengel's deformity	3
Other bones	3
Central nervous system	58
Cerebrum	20
Cerebellum and brain stem (including 20 cases of Arnold-Chiari malformation)	26
Other portions	12
Hernia	27
Dislocated hip	23
Pilonidal sinus	13
Genitourinary anomaly	11
Congenital heart disease	4
Other anomalies	30
Total	570

or receiving post-mortem examination. Thus, relatively few patients with myelocoele have been autopsied, but of these a high percentage have shown associated cerebellar or brain-stem anomalies. It seems likely that if more autopsy material were available, more such anomalies would have been found.

It will be noted that several of the commoner associated anomalies may have been secondary to the spinal-cord lesions, for example, club feet, dislocated hips and hydrocephalus.

CLASSIFICATION

We have utilized the commonly accepted terminology but have added three subdivisions of our own. We have been constantly impressed by the association of spina bifida and meningeal defects with an overgrowth of fatty tissue. These lipomatous tumors consist of lobules of gritty, firm fat, bound together by fibrous septums, and are usually adherent to adjacent fascial (or dural) planes by firm and often vascular attachments. If a meningeal defect coexists, these tumors may extend intrathecally for some distance, even causing intrinsic compression on the nerves or cord. If such a tumor is present with spina bifida occulta, we have used the term "lipoma." If a meningeal sac is present as well but no nerve elements are involved, we have called the condition a "lipomeningocele." If nerve elements are also involved, we have used the term "lipomyelomeningocele."

All meningeal protrusions, whether or not associated with nerve tissue, whose osseous defect was in the skull (cranium bifidum) we have grouped together as "encephalocele." Simple dermoid cysts arising from the dura and extending through the bone have been excluded.

Often classification of a lesion from the data available in the record is difficult. When surgical or pathological data are available, diagnosis can be accurate, but the clinical distinction between a meningocele and a myelomeningocele is often per-

TABLE 3. Incidence of Lesions

TYPE OF LESION	NO OF CASES
Spina bifida occulta (13 with lipoma)	69
Meningocele	98
Lipomeningocele	14
Myelomeningocele	279
Lipomyelomeningocele	18
Encephalocele	84
Total	558

plexing. We have therefore adopted the following criteria. If a sac exists clinically and nerve elements cannot be seen, and if there is no evidence of neurologic disability as demonstrated by muscular weakness or paresis, loss of sphincter tone or aberration in cutaneous sensation, the lesion is a meningocele. If nerve elements are visible or neurologic disability exists, the lesion is a myelomeningocele.

With these criteria, the relative frequencies of the different types of lesion are shown in Table 3

SITE AND AGE

Table 4 records the site in which these lesions were found. Six patients suffered from multiple defects, and 2 of these had three separate lesions

TABLE 4 Site of Lesion

TYPE ACCORDING TO SITE	NO OF CASES
Cranial	84
Nasal	5
Nasopharyngeal	1
Frontal	6
Lacrimal	9
Occipital	63
Cervical	23
Thoracic	39
Thoracolumbar	43
Lumbar	205
Lumbosacral	87
Sacral	46
Thoracolumbosacral	10
Undesignated	8
Pelvic	1
Total	546

The age at which the patient was first seen is of some interest (Table 5). As would be ex-

pected, the majority of the patients were seen in the first year of life. In these the local mass or deformity was the presenting complaint. In 42 patients, the chief trouble was orthopedic, whereas

TABLE 5. Age of Patients when First Seen.

AGE	No OF CASES
Less than 1 week	102
1-3 weeks	180
1-11 months	179
1 year	29
2-4 years	30
5-11 years	26
Total	546

14 complained initially of urinary difficulties. Many of these patients were well along into childhood before increasing neurologic disability led them to seek aid. In 16 patients, spina bifida occulta was found as a fact unrelated to the admitting complaint.

Among the patients with encephalocele there was a great deal of variation in the size, site and amount of neural tissue involved, and these factors are of prognostic significance. If a protrusion consists only of dura containing fluid attached by a pedicle, its size is of slight importance, large ones being as readily removed as smaller ones. If, however, the sac contains a neural mass, and particularly if the ventricular system is demonstrated by pneumoencephalographic studies to extend into this mass, the prognosis is usually poor. Nevertheless, occasionally a sac contains anomalous, abnormal neural tissue that can be excised with impunity. We have found that lesions in the occipital region more frequently contain neural elements and if so offer a poorer prognosis than do lesions in other sites, even though they are small. This is apparently because such lesions are frequently associated with a malformation at the base of the brain, which leads to a block of the flow of cerebrospinal fluid and to hydrocephalus, and the latter proves fatal whether or not the lesion is removed. Associated anomalies of the brain are occasionally found even with apparently hopeful lesions in all sites, so that prognosis must be guarded.

In our operative technic the sac is developed to its base, excised together with its neural contents, and the dura tightly closed. A firm closure of the soft tissues and skin is considered imperative. No attempt is made to repair the bony defect.

The results obtained by operation for encephalocele are, on the whole, encouraging. In our series 59 patients had adequate follow-up studies. Of these, 52 underwent operation, and 17 (33 per cent) of them subsequently died, either in the im-

mediate postoperative period or at some later date. Twenty-one (34 per cent) of the 59 patients are alive, well and *entirely normal*. One of these when last heard from was playing football on his high-school team. When one sees a photograph of this boy as a baby with a sac almost as large as his head protruding from the occiput, this result becomes even more impressive. Other results are equally striking. Table 6 lists the present status of our 84 patients with encephalocele. From these data it seems fair to conclude that about a third of the patients with encephalocele can, with the aid of operative therapy, look forward to an entirely normal existence.

Spina Bifida

Because the complaints and the degree of disability of patients with spina bifida are so varied, classification for analysis of a large group presents

TABLE 6. Present Status of Patients with Cranium Bifidum.

STATUS	No OF CASES
Alive	37
Operated on	35
Normal	20
Mental retardation	6
Increasing hydrocephalus	4
Associated anomaly	5
Unoperated on	2
Dead	22
Operated on	17
Unoperated on	5
Unknown	25
Total	84

many difficulties. It seems as if each patient were almost a law unto himself. It appeared, however, that in the absence of a leak in spinal fluid, with its concomitant danger of infection, there are two major factors that constitute a threat to the patient's life and health: hydrocephalus and injury to, or the lack of, the neural elements of the vertebral canal. The former is recognized by an enlargement of the head, undue separation of sutures and tense fontanelles; the latter by muscular paresis or weakness, lack of sphincter tone and loss of cutaneous sensation. The presence of any one of the latter or a combination of them we have termed "neurologic disability." We have found patients who have had all possible combinations of these two factors, but by utilizing them as a means to classification we can introduce some order into an otherwise chaotic situation. Nor is this division unduly arbitrary, since it parallels, to a certain extent, clinical thought in evaluating these patients as operative risks.

In the operative mortality and postoperative results any series of cases of spina bifida depends on the indications for operation. Does the presence

of increasing neurologic disability—progressive incontinence, for example—constitute an indication for or against operation? Does the presence of hydrocephalus contraindicate operation? What aspects of the local lesion constitute operative indications? On the answer to these questions there seems to be no general agreement. At the Children's Hospital in recent years all cases of spina bifida have been under the care of the Neurosurgical Service and certain concepts of operability have been elaborated.

The presence of a mass constitutes an indication for operation in most cases. Occasionally a small lipomatous tumor is found with occult spina bifida and no neurologic disability, and in such cases operative interference is not necessary. The age of choice for operations in infants is between twelve and eighteen months. This allows time for the development and recognition of disabilities and hydrocephalus, for the local growth of skin adequate to permit closure and for the child to develop in stature and nutrition into a better operative risk. However, certain local considerations may alter the desirability of waiting. If the sac is broken but uninfected, or if it is so thin as to threaten rupture at any moment, and the patient appears to be otherwise relatively normal, immediate operation is demanded to save his life. The presence of infection of the sac or of meningitis contraindicates operation, but local dressings and chemotherapy may suffice to overcome the infection.

Assuming that the mass does not threaten rupture, the patient can be cared for adequately on the following regime. The mass and surrounding skin are thoroughly washed with boric solution and a sheet of perforated Cilkloid applied. A "doughnut" of sheet wadding wrapped in gauze is placed around the lesion for protection. Over the top is placed one or two gauze pads, and the whole is bound to the infant by a flannel or linen binder. The Cilkloid is replaced by the mother as necessary but not too often, since frequent changing nullifies the stimulative effect on epithelial proliferation. The lesion is washed daily with boric solution and clean gauze is reapplied. Every one or two months the patient visits the hospital, where progress is evaluated.

The presence of progressive hydrocephalus constitutes a contraindication to operation. Occasionally hydrocephalus stabilizes, and if this occurs, the contraindication no longer exists.

The presence of neurologic disability does *not* necessarily constitute a contraindication; indeed, particularly in the older age group, if such disability is progressive, we believe that it is a strong argument for operation. In many of these patients, owing to their defect, the spinal cord becomes

anchored at this site. As the child grows tension is placed on the cord, since it increases in length less rapidly than the vertebral canal. There may also be local compression by lipoid tumor growth. Both these elements contribute to the development of the signs of nerve dysfunction. This usually occurs between the ages of six and ten. In such cases, the wisest procedure is exploratory laminectomy with a view to alleviating, if possible, the local situation. This attempt is occasionally successful.

The decision to operate having been made, certain technical phases of the operative procedure are of paramount importance. The skin preparation must be wide and thorough. We use a colored chemical disinfectant, such as diluted tincture of iodine or Tincture Merthiolate, as the final step in the preparation, thus making the cleansed field visible and assuring a wide enough area. The incision, which is usually elliptical, is made with the long axis transverse. Where the lesion is low, the incision must be placed high enough to avoid the intergluteal fold. We always wall off the lower limit of the field from the region of the anus by a sheet of sterile gutta percha before the drapes are placed, and postoperatively by a sheet of rubberized silk attached by adhesive strapping. The sac is traced to its emergence from the bony canal, as much as possible is excised, and a tight closure of the dura is made. For this we use interrupted sutures of fine silk, and make the closure as near watertight as possible. Meticulous care must be taken not to cut or injure nerve elements that may be adherent to or contained within the sac. If need be, these are carefully dissected free and returned to their position within the canal. No attempt whatsoever is made to repair the bony defect. If the cut edges of the fascia of the erector spinae muscle come together easily, they are approximated, but the repair of this layer is of no great importance, and under no circumstances should such great effort be made as to cause compression on the underlying dural closure. A firm repair of the subcutaneous tissues and skin is of great importance. The skin must be made to approximate without undue tension by means of wide undermining of flaps and even relaxing incisions at a distance, if such are necessary. Silver foil is placed over the wound, and a compression bandage applied. For this we have found several layers of gauze held in place by Elastoplast bandage quite satisfactory. For several days postoperatively the patient is held prone on a Bradford frame with the head end about 10 cm. lower than the foot. This position probably minimizes the pressure of cerebrospinal fluid on the dural suture line during the healing period, and thus reduces the possibility of the

development of a leak. Unless there is some indication for doing so, the wound is not disturbed for six or seven days, at which time the sutures can be removed.

Table 7 gives a somewhat detailed listing of the present status of our 462 patients with spina bifida

TABLE 7. *Present Status of Patients with Spina Bifida*

	No. of Cases
Alive	234
Unoperated on	74
Normal	11
With spina bifida occulta	8
With associated small lipoid tumors	3
Abnormal	63
Awaiting operation, no neurologic disability	3
Awaiting operation, neurologic disability	17
Operation not advised	38
Neurologic status normal (associated anomaly)	5
Operated on (Children's Hospital)	148
No hydrocephalus and no neurologic disability preoperatively	84
Entirely normal	45
Developed hydrocephalus (now stabilizing)	5
Developed neurologic disability (Severely incapacitated 8, mildly incapacitated, 15, disability immediately post-operatively 10, disability months or years later 13)	23
Developed both hydrocephalus and neurologic disability	4
Normal as regards spina bifida associated anomaly	7
No hydrocephalus but neurologic disability preoperatively	48
Improved by operation	9
Made worse by operation	4
Neurologic disability persists (severe 25 mild 6)	31
Developed hydrocephalus	4
Hydrocephalus but no neurologic disability preoperatively	7
Arrested (normal 1 mild neurologic disability 5)	6
Progressing	1
Hydrocephalus and neurologic disability preoperatively	9
Arrested (severe 7 mild neurologic disability 2)	9
Progressing	0
Operated on elsewhere (severe 10, mild neurologic disability 2)	12
Dead	167
Unoperated on	127
Operated on	40
Operative deaths (meningitis 12)	22
Subsequent deaths (hydrocephalus 16)	18
Status unknown	61
Total	462

The data presented in Tables 7 and 8 allow some interesting conclusions. There are 401 patients whose status is known and whose follow-up studies are considered adequate. Of these, 234 (58 per cent) are alive. The remainder have died of a variety of causes. Operation was performed on 158, and 20 more are awaiting operation. Thus, 208 (52 per cent) were or are thought to be suitable for operation. The immediate operative mortality in our hands was 12 per cent.

Of the patients who survived, 60 are considered normal and 61 are suffering from neurologic

TABLE 8. *Present Status of Surviving Patients*

PATIENTS	NORMAL	MILD NEUROLOGIC DISABILITY	SEVERE NEUROLOGIC DISABILITY
Operated on (Children's Hospital)	46	42	60
Others	14	19	53
Totals	60	61	113

mild disability. The patients in both these groups may be considered as capable of leading a normal human existence. Thus, about 30 per cent of the patients with spina bifida may look forward to a life unhampered by any significant incapacity resulting from their anomaly.

Congenital lack of neural elements or destruction by long standing compression results in neuro disability of an irreversible nature. One of these situations prevails, unfortunately, in the majority of cases where disability is present. However, occasionally local compression or traction on the cord is the cause of the progression of symptoms. If these are recognized, laminectomy offers promise of relief if the local situation permits operation. In our series there were 10 patients in whom relief or improvement in neurologic disability occurred following such an exploration.

In the light of the data presented by this review, we believe that an outlook of extreme pessimism in the presence of spina bifida is unwarranted. Each patient must be evaluated as an individual problem.

SUMMARY

A series of 462 cases of spina bifida and 84 of cranium bifidum (encephalocele) is presented, with data on the incidence, sex, race, type, site, associated anomalies and clinical manifestations.

Therapeutic indications and end results are tabulated and discussed.

Thirty per cent of patients with spina bifida and 34 per cent with encephalocele may expect a relatively normal life. An unduly pessimistic prognosis is therefore unwarranted until individual evaluation has been carefully pursued.

Any further simplification, however, would deprive it of analytic value.

A portion of this material is presented in condensed form in Table 8, which gives only the present status of the living patients grading them as normal, slightly handicapped or severely handicapped.

SPASMODIC RECTAL PAIN

A Review of the Literature and Report of a Case

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SPASMODIC pain in the rectum, which is localized a short distance above the sphincter ani, has received scant attention in the literature. It appears without warning, is slightly gnawing at first, but increases steadily in intensity to a point that may cause loss of consciousness, then slowly disappears, leaving no ill effects except a sense of fatigue. The average attack lasts for about fifteen minutes. The patient has a sensation of uneasiness at the anus, with a tightening sensation at the anal canal. A continuous dull ache is felt in the rectum, as though it were ballooning out. This neuralgic type of pain is not related to the intake of food, the type of food ingested or bowel function. It is about twice as common in men as in women.

The commanding character of the pain and the unknown etiology entitle the condition, often called "proctalgia fugax," to be considered a definite entity. As early as 1917, MacLennan,¹ of Glasgow, gave an excellent description of the condition. Later Thaysen,² of Copenhagen, and Stolte³ wrote articles that added much information and stimulated many physicians to send letters concerning cases that had come to their attention. Many of these letters were published in the *Lancet* during 1935.⁴ These represent many opinions regarding the etiology of the disease, but not one contains a description of the sigmoidoscopic examination during the attack. The following case report is therefore of interest because I was able to perform such an examination.

CASE REPORT

T. H. S., a 60-year-old man, in good general physical condition, had suffered repeated attacks of rectal pain, occurring at intervals during the previous 4 years. The pain, gnawing in character, awakened him from a sound sleep. It began gradually, and the rectum seemed to be slowly ballooning out. The pain increased in severity and seemed to involve an area in the rectum "about 5 inches long." Slight spasm was noted in the area of most intense pain. Regardless of change of position, the patient continued to suffer acute distress. Efforts at micturition and defecation were unavailing, although the patient stated that he thought he would obtain relief if he could pass urine or gas.

After 15 minutes or so, the pain gradually subsided. The patient felt no ill effects except a feeling of lassitude. He was able to go to sleep readily after each attack, and had no subsequent awakening during the remainder of

the night. Attacks came at intervals of about three months, but never in the daytime.

During an attack on July 26, 1942, a rectal examination was made, and proved enlightening. Digital examination revealed slight rigidity of the muscles of the rectum, and the mucosa of the anal canal felt hot, as though inflammation were present. The pain persisted. The prostate gland was enlarged. Insertion of the anoscope revealed the presence of a few small hemorrhoids. The mucosa was bright red.

Through the sigmoidoscope the rectal mucosa appeared redder than normal, and resembled that seen following prolonged or rough massage of the prostate gland. It seemed swollen, and the vessels were more prominent than normal. The site of the pain was at the central portion of the levator ani muscle, and slight pressure exerted by the tip of the instrument at this point caused mild spasm. No ulcerations were noted. The middle valve of Houston was more rounded than normal and the superficial vessels more pronounced. As the instrument reached the rectosigmoidal angle, some difficulty was encountered in locating the lumen of the bowel. At this point, with the passage of a considerable amount of gas, the patient noted relief of the pain. As the sigmoid was approached, normal mucosa came into vision. Prostatic massage was done, and repeated three days later.

Sigmoidoscopic examination a week after this attack showed the mucosa of the anal canal to be still bright red. The rectal mucosa was pink, much paler than when seen during the painful episode. The veins were not engorged. In fact, the picture was that of a normal rectum.

In all, 12 cases of spasmodic rectal pain have come under my observation — 10 in men and 2 in women. All the men had prostatic hypertrophy and both women had pelvic inflammation. Many hypotheses concerning the etiology of the condition have appeared in the literature, but any connection between rectal spasm and prostatic hypertrophy in the male or pelvic disease in the female has for the most part been disregarded. Beckman⁵ stated in passing that his patient had had prostatic massage before his attack, but ascribed the condition to excessive smoking. The seizures simulated those occurring in certain types of "pseudo-angina," which clear up when the patients forego the use of tobacco.

All authors agree that proctalgia fugax is a rectal rather than an anal phenomenon. Attacks occur at night, as a rule, and during periods of fatigue and stress. No rectal disease is found, although in some cases hemorrhoids are present. The pain is similar to that of tension, contraction or even incision, accompanied by a sensation of pressure. The attacks are not followed or preceded by a desire to

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defecate. As a rule, if they are frequent they are less severe. In 2 of 9 cases reported by Thaysen,² there was a family history of the condition, one or both parents suffering similar attacks.

Stolte³ believes that the pain is of nervous origin and is due to spasm. It does not occur in the sphincter ani, and anal spasm is always secondary. All patients are sure that the pain is above the anus. According to Smith,⁴ when the examining fingertip touched the fibers of the levator ani muscle, the patient said, "That's the spot where I get the pain."

Thaysen² and others consider it a spasm of the rectal musculature. MacLennan¹ and Abrahams⁴ believe that the lesion is the result of a neurosis, although it affects many persons of a non-neurotic temperament. Smith⁴ states that pain is due to a cramp of the levator ani muscle and gives the following reasons: the pain is analogous in character to muscle cramp elsewhere in the body; it has a tendency to spread and to involve the entire muscle; it occurs during periods of fatigue; it is prone to arise in a muscle that has recently been excited; it appears when the patient is getting warm in bed, as is the case with cramps in other muscles; and victims have obtained relief by stretching while assuming a squatting position.

Ryle⁴ associates the attacks with mental or physical fatigue. Mummery (quoted by Ryle) regards the disease as a tic. The pain has been associated with sexual excitement, masturbation, migraine and epilepsy (Carlill⁴). A woman patient stated that attacks always occurred just before or just after menstruation (Tecon⁴), but no pelvic disease could be discovered. Yeomans⁵ reported 2 cases, both in women. No pelvic disease could be found in one; the other patient had been operated on for anal fissure, with a deep incision through the levator ani muscle in the posterior commissure. Thus a nerve filament might have been caught in the extensive scar. However, no relief followed when the scar was dissected out.

A review of the innervation of the rectum and anus in the light of the symptomatology indicates that the site of the pain is in the rectum, as all the patients insist. The tissues above the pectinate line are supplied entirely by the sympathetic system, whereas below, in the anal region, the tissues are supplied by spinal nerves and also by some fibers from the sympathetic nerves. Above the line (in the rectum), the ordinary sensations such as touch, pain and heat or cold are not found to any degree, and usually are not present at all; but there are sensations of pressure and muscle sense.

Inspection of the anal area frequently affords considerable information concerning whether the irritation is in the anal segment, innervated by the spinal nerves, or in the rectum, innervated by the sympathetic nerves. With infection, irritation or trauma of the portion below the anorectal line, spasm of the sphincter muscles and contraction of the anal aperture are the rule. A rectal lesion—that is, one above the line—is frequently associated, not with spasm of the muscles, but with a pathological condition and relaxation of the anal ring (Martin⁶).

Inflation of the rectum with air has been advocated by Ryle,⁴ Marshall⁴ and others. Locally, applications of heat, as by a sitz bath or enema, and the insertion of various kinds of suppositories have been employed with good effect. Mummery⁴ uses alcohol injection, since he believes the condition to be a tic of the sacral plexus. Yeomans⁵ injects 30 cc. of a 1 per cent solution of novocain into the sacral canal, followed by 30 cc. of 25 per cent alcohol if the relief is only temporary. Moltke (quoted by Thaysen²) suggests amyl nitrite, because the nitrites have been employed successfully for other spastic affections of the bowels, and also because, if efficacious, it would prove that the condition is primarily due to spasm. Tecon employs short-wave diathermy. Beckman⁷ mentions the possibility of an allergic factor and points out that in 2 cases Rowe's elimination diets were of help. Often, however, the attack ceases spontaneously before the patient has had time to try any specific remedy. No sequelae have been noted, and the condition has a tendency to improve with advancing age. For this reason Hanssen (quoted by Thaysen²) classified proctalgia fugax as a minor complaint, but admitted that attacks might be severe enough for it to be considered a distinct entity.

DIFFERENTIAL DIAGNOSIS

The attacks of proctalgia fugax are different from the crises of tabes dorsalis, and indeed no patient with this complaint has been tabetic. The former attacks are fleeting, occurring at widely spaced intervals. Those of tabes are accompanied by watery and frequent stools, hemorrhage from the anus and tenesmus. The pain radiates, whereas in proctalgia fugax, as Ryle⁴ and Stolte³ have demonstrated, it is definitely localized in the levator ani muscle.

Proctalgia fugax also differs from the nervous type of rectal pain called enteralgia, or neuralgia of the mesenteric plexus. In the latter condition, attacks may last for several days, the pain radiates, and the attack is often preceded or followed

by abdominal pain. It may be part of a syndrome due to lead colic, colitis or even duodenal ulcer.

The pain differs also from that of coccygodynia. In the latter, patients are most uncomfortable in the sitting posture, and there is a dull ache at the base of the spine. Manipulation and massage improve the condition. With proctalgia fugax, the patient is loath or unable to move because of the excruciating spasm. Also proctalgia fugax is commoner in men, but coccygodynia in women.⁸

A cardinal reason for establishing the correct diagnosis in these cases is the need of reassuring these patients that they do not have cancer of the rectum. Sigmoidoscopic examination will dissipate this fear and give them confidence. Therefore, even though the symptom-complex of proctalgia fugax is not treated by such authorities as Nothnagel, von Bergmann, French, Babcock, Naegeli, Buie and others (as mentioned by Thaysen²), the condition merits more attention, and is

commoner than the reports in the literature lead one to believe.

SUMMARY

A case of spasmodic rectal pain is reported, and the etiology, diagnosis and treatment of this condition are discussed.

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CLINICAL NOTE

ACUTE HEMOLYTIC ANEMIA FOLLOWING SULFADIAZINE*

REPORT OF A CASE

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ACUTE hemolytic anemia is an important toxic effect following treatment with the sulfonamides. The incidence following sulfanilamide is 1 to 2 per cent and following sulfapyridine 2 to 3 per cent.¹ It is apparently quite rare following sulfathiazole. Spink² reported that he had not encountered acute anemia in over 400 patients treated with sulfathiazole. So far as I am aware, acute hemolytic anemia following sulfadiazine has not yet been reported.

CASE REPORT

L. F., a 65-year-old woman, entered the Evans Memorial on September 7, 1942, complaining of dyspnea of 4 days' duration. She had been subject to attacks of "bronchitis" with cough and fever each winter for many years but had had no dyspnea, chest pain or edema. She had never taken any of the sulfonamides. The present illness began rather abruptly with increasing dyspnea and asthmatic breathing accompanied by rapid irregular heart action.

Physical examination revealed an obese woman in moderate respiratory distress. The heart was enlarged to the

left, the rhythm was grossly irregular at a rate of 130 a minute, and there was a moderately loud apical systolic murmur. The blood pressure was 230/140. There were moist rales at both lung bases but no venous distention, liver engorgement or edema.

The patient improved satisfactorily on the usual regime of rest, sedation with barbiturate, digitalis and intravenous Mercupurin. On the 11th hospital day, after a completely afebrile course, her temperature rose, she complained of slight pain in the right lower chest, and the respirations rose to 32. There was no cough or hemoptysis. Examination of the chest revealed a moderate number of coarse crepitant rales at the right lung base. A roentgenogram showed patches of increased density at the right lung base, which were interpreted as either a pneumonic process or multiple infarcts. The white-cell count rose to 17,000. Because of the history of recurrent bronchitis and uncertainty concerning the etiology of the lung disease, she was started on sulfadiazine by mouth. The dosage of the drug and the patient's clinical course are shown in Figure 1.

Two days after the institution of sulfadiazine therapy the erythrocyte count had fallen from 4,200,000 to 2,200,000, with a corresponding fall of the hemoglobin from 12.5 to 8.1 gm. The patient became slightly icteric, but this might well have been assigned to the pulmonary infarction, which was subsequently clearly indicated by the appearance of hemoptysis and signs of phlebotrombosis of the right leg. There was no striking pallor to give warning of the precipitous drop in erythrocyte count or hemoglobin. The liver and spleen were not palpable, and there was no nausea, vomiting or skin eruption. The white-cell count showed neither a tendency toward leukopenia nor one toward the hyperleukocytosis seen in some cases of acute hemolytic anemia following the administration of sulfonamides. Despite increasing amounts of fluid the urinary output fell and there was a slight rise in the blood nonprotein nitrogen, but there was no hematuria or crystallinuria. The drug was discontinued, fluids were forced, and the patient was given

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transfusion of 500 cc of whole blood. Meanwhile, slight tenderness had been noted in the right calf. The femoral

the previous levels, and the subsequent course was satisfactory.

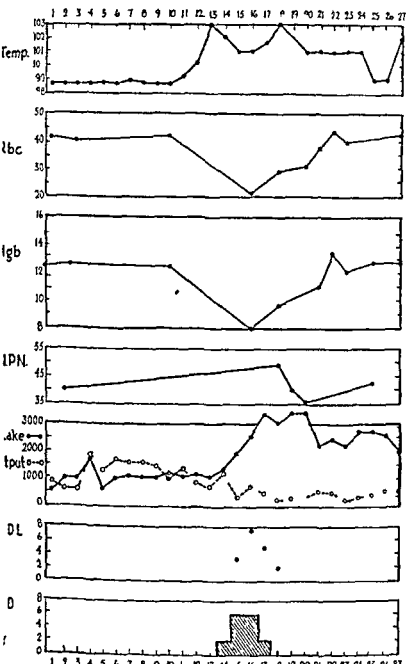


FIGURE 1 Course of Acute Anemia Developing during the Administration of Sulfadiazine

The temperature is expressed in °F, the red-cell count in number $\times 10^6$, the hemoglobin in gm per 100 cc, the nonprotein nitrogen in mg per 100 cc, the intake and output in cc, the sulfadiazine blood level in mg per 100 cc, and the sulfadiazine dosage in gm.

vein was opened and a large loosely adherent clot removed, following which the vein was ligated. The erythrocyte count and hemoglobin value quickly returned to

Although sulfadiazine is undoubtedly less toxic than the other commonly employed sulfonamides, vigilance during its administration must not be relaxed. The present tendency to widespread use of sulfadiazine without adequate laboratory control in the home, for example, is certain to result in tragic consequences sooner or later. In the present case there were no alarming clinical manifestations to warn of the serious, acute anemia. Certain of the toxic reactions may develop very rapidly in the first few days of treatment, and it is probable that as more of the population becomes exposed to the sulfonamides, accelerated reactions due to the development of hypersensitivity to the drug will become commoner. Sulfadiazine had been used in the treatment of over 250 patients in this hospital before this case was encountered. At best, this affords a rough estimate of the incidence of acute hemolytic anemia, but it suggests that it may be no less and possibly somewhat more frequent following sulfadiazine than following sulfathiazole therapy.

The oliguria and elevated blood nonprotein nitrogen in the present case may also have been a direct toxic manifestation of sulfadiazine, but in the absence of hematuria or crystalluria it seems more likely that the renal complications were a manifestation of hemoglobinuria, although there is no proof that the latter occurred. It is probable that in rare cases the sulfonamides may produce oliguria without signs of renal irritation and in the absence of significant crystalluria.

SUMMARY

A case of acute anemia following the administration of sulfadiazine is reported.
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MEDICAL PROGRESS

HERPES ZOSTER

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THE accumulated evidence supports the opinion that herpes zoster is essentially an acute posterior poliomyelitis¹ due to the virus of chicken pox and unrelated to the virus of herpes simplex. Although anatomically the root ganglions are placed outside the spinal cord, they consist of cells that have migrated from the posterior horn, and in this way their constant involvement may be accounted for. The inflammatory changes found in the anterior horn by Lhermitte² and others are presumably due to the spread of the virus from the posterior horn, and explain the occasional occurrence of muscular paralyses^{1, 3} in a disease that primarily involves the sensory system.

PATHOLOGIC PHYSIOLOGY

The pathologic physiology of herpes zoster involves a consideration of all agents that may produce any type of injury to the dorsal-root ganglions. These include pressure of tumors, traumatic injuries, exudates of systemic diseases (syphilis), poisoning by heavy metals (arsenic), leukemia and other blood dyscrasias, Hodgkin's disease and vertebral diseases. It has been suggested that these conditions are only predisposing causes, for the zoster follows its normal course, heals and does not recur despite the continued presence of these factors.⁴

The mechanism of production of the distinctive skin lesions of herpes zoster is of considerable clinical interest. The pathologic physiology involved has been well understood for many years but deserves a brief review. Wright⁵ has recently given an admirable summary of this subject. Stimulation of the peripheral end of the cut posterior nerve root produces vasodilatation of the corresponding segments of the skin and muscles. According to Lewis,⁶ the vasodilator fibers in the sensory nerves act by liberating a substance ("H-substance") resembling histamine in its properties. It is suggested (arguing from the analogy of the action of histamine) that the H substance dilates the capillaries by direct action on their walls, but that the arteriolar dilatation is due to an axon reflex. The H substance stimulates sen-

sory nerve endings in the skin and impulses pass back along afferent nerve fibers, but the impulses make none of the usual circuits through the central nervous system, and after traveling only a short distance reach branching nerve-fiber junctions and turn peripherally again along branches that reach and dilate neighboring blood vessels. The sensory fibers arising from pacinian and other nerve endings in the skin have been shown to extend numerous collaterals to the adventitia of the neighboring arterioles, and these fibers are believed to be responsible for the dilator effects just described.

To continue one's reasoning along the above lines, in herpes zoster, injurious influences, such as inflammation, hemorrhage, pressure and poisons, act on the posterior-root ganglions or their cranial homologues. These processes lead to stimulation of the ganglions and have an effect equivalent to stimulation of the peripheral ends of the cut posterior nerve roots. As a consequence, dilatation of blood vessels occurs in patches along the distribution of the involved sensory nerves. Antidromic impulses traveling along these nerves release the H substance, which dilates the capillaries and sets up an axon reflex that in turn dilates the arterioles. The H substance not only dilates the minute blood vessels but also increases their permeability. This increase causes the exudation of serum and formation of vesicles within areas of erythema (vasodilatation) along the distribution of the posterior nerve roots of their cutaneous sensory branches.

Head and Campbell⁷ as well as Lewis and Marvin⁸ believe that the eruption of zoster is due to antidromic impulses passing down sensory nerves to the skin, as just described. Stern,⁹ on the other hand, has proposed the theory that the eruption of zoster is due to the passage of causative organisms down sensory nerves to the skin. In support of this interpretation may be quoted the work of Kundratitz,¹⁰ Bruusgaard,¹¹ Paschen¹² and Amies,¹³ who have produced evidence that a virus is present in the vesicles of zoster.

The skin eruption of herpes zoster may be explained by the above physiologic mechanisms. The essential unit is a cluster of vesicles situated on a basic plaque of erythema. Several such clusters

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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are usually present and may involve any part of the body. The vesicles themselves are ordinarily tense and thick walled.

The pain of herpes zoster is easily accounted for on the basis of inflammation or degeneration of sensory-nerve fibers entering the involved dorsal root ganglions. This pain may be severe or may be entirely absent. It may precede and accompany the skin manifestation and, especially in elderly patients, it may occur as a severe and intractable neuralgia persisting for months or years after disappearance of the skin lesions (post herpetic neuralgia).

Herpes zoster is especially frequent in persons who are overworked or ill. The appearance of the eruption is usually preceded by malaise, neuralgic pain and hyperesthesia of the affected area. The disease runs an acute course lasting from ten to thirty days. One attack almost always confers immunity. Second attacks may occur but are very rare. Many kinds of irritation and damage can precipitate an attack of zoster, "possibly through activation or stimulation of the dormant virus or through reduction of the delicately adjusted factors conferring host immunity or local resistance."¹⁴ The commonest "trigger factors" include the following: drugs, such as arsenic, lead, bismuth, mercury, iodides, gold, morphine, carbon dioxide and carbon monoxide; blood dyscrasia, especially leukemia; trauma; infectious diseases, such as influenza, encephalitis, erysipelas, tuberculosis and syphilis, particularly early cardiovascular syphilis, paresis and tabes; vaccination, and malignant tumors and Hodgkin's disease, which act either by pressure on the ganglions or by toxic effect.

DIAGNOSIS

The typical case of herpes zoster presents no diagnostic difficulties. If, however, the vesicles are confined to some obscure locality such as the ear canal or bladder, and if they remain undetected, it may not be possible to diagnose the disease on the basis of pain and other symptoms. Some observers believe that zoster may occur without skin manifestations. In such cases, the diagnosis may be difficult to distinguish from other types of neuralgia, although a lumbar puncture disclosing the characteristic zoster lymphocytosis of the spinal fluid may be of considerable help. In the early stages of zoster one may encounter cases where there is erythema but no pain or vesicles. Here the diagnosis is not always easy, but the patchy character and unilateral distribution of the erythema should be helpful. The characteristic vesicular plaques of herpes zoster usually appear suddenly and acutely—either one by one or all together.

The eruption may take three or four days to become complete, but sometimes new plaques appear as long as two weeks after the onset. *Lymph node enlargement is frequent.*

In the differential diagnosis of herpes zoster it is well to remember that the pain may precede the appearance of cutaneous changes and may lead to errors of diagnosis. It may simulate the pain of pleurisy, gall-bladder colic, kidney stone colic, appendicitis, myositis or neuritis.¹⁵

The specialist must recognize not only the usual type of herpes zoster but its less common variations such as the gangrenous, hemorrhagic, bullous, bilateral and generalized types.¹⁶ In the gangrenous type, necrotic and destructive lesions occur in what is usually a severe form of the disease. This may happen in any region but is commonest in the ophthalmic area, the cornea frequently being severely involved. Bilateral zoster may be symmetrical or asymmetrical; it is extremely rare and, contrary to lay belief, is not fatal. Excellent illustrations of bilateral herpes zoster are given by Sutton and Sutton.¹⁶ Bilateral herpes zoster involving both trigeminal ganglions has been described by Campbell.¹⁷ Extensive herpes zoster in patients suffering from rheumatoid purpura has been reported by Audibert and Paganelli.¹⁸

Thirty-two cases of generalized zoster in association with leukemia have appeared in the literature. The first such case was reported by Fischl¹⁹ in 1913. The most recent of these cases have been reported by Wile and Holman,²⁰ who analyzed all the cases previously described and tabulated their salient features. They found that in 93 per cent the leukemia was lymphatic in type, and that in 71 per cent the patients were men averaging sixty years of age.

Generalized zoster may also occur without association with leukemia. In this interesting form of the disease one finds scattered discrete papular and vesicular lesions, which are usually accompanied by headache, fever and malaise. There are often mucous membrane lesions and the entire picture is quite similar to that of chicken pox. Only epidemiologic considerations and the presence of a concomitant typical herpes zoster along the course of a nerve permit differentiation from ordinary chicken pox.^{21, 22}

Besides the bilateral and generalized forms of herpes zoster, another rare variation is the unilateral type with multiple lesions. Because of its rarity, Walls²² has reported an example. Most of the reported cases with multiple lesions have occurred in association with severe constitutional illnesses, such as leukemia, Hodgkin's disease and tuberculosis. Presumably in these cases the virus

of zoster may find a vulnerable ground to work on. Walls's patient, on the contrary, was a boy of nineteen in excellent health. He exhibited a typical well-marked, grouped, vesicular rash sweeping around the left side of the chest in the segmental distribution of the sixth dorsal segment. In addition a narrow strip of grouped vesicles extended from below the tip of the acromium down the outer front of the left arm, corresponding to the skin distribution of the fifth and sixth dorsal segments. Furthermore, a similar rash on the left thigh corresponded anatomically with the skin distribution of the third lumbar segment. Finally, there was a group of vesicles on the outer half of the left popliteal fossa traveling down the outer aspect and front of the leg, corresponding to the skin distribution of the fifth lumbar segment. This patient therefore presented four distinct areas of skin involvement, a distribution equally as bizarre as the spinal-cord involvement must have been. The fourth lumbar segment was completely missed but the ganglions both above and below were involved. The patient's general condition was excellent, there being no pyrexia or changes in the nervous system; in fact, he was not sufficiently ill to require hospitalization.

Herpes zoster may occur in childhood. Koch²³ reported a case in a boy of five and a half and Batignani²⁴ one in a newborn infant whose mother had the disease at parturition. Bruce²⁵ reports that ocular complications occur in about 50 per cent of all cases in childhood, and he has made an interesting review of herpes zoster of the eye in childhood. He describes in detail the morphology of the eruption as it affects the cutaneous surface of the eyelids, the bulbar and palpebral conjunctiva and the cornea itself. The cornea loses its sensitivity early in the course of ophthalmic zoster. Minute subepithelial dots appear, often coalescing to form large areas of infiltration. Subsequent scarring may lead to serious impairment of vision. The iris is always inflamed if keratitis is present, and this iritis may actually be due to localized herpetic eruptions on the surface of its stroma. In such cases the inflammation is apt to be severe, glaucoma may supervene, and the eye may be lost.

In childhood zoster of the eye, the ocular muscles are attacked singly or in groups in about 7 per cent of all cases, according to Bruce.²⁵ Complete ophthalmoplegia may be accompanied by exophthalmos. This has been ascribed by some writers to atony of the muscles, and by others to sympathetic stimulation.²⁶ Ptosis may be either apparent, produced by the weight of the swollen lid, or real, as a result of third-nerve paralysis. Accommodation is paralyzed in some cases. As a rule, the prognosis is good and muscular balance

is restored in about six weeks. The optic nerve is rarely involved, but if it is, a severe neuritis followed by atrophy may result.²⁷

Herpes zoster following lumbar puncture has been described by Carter.²⁸ In a case of syphilis of the central nervous system, a lumbar puncture was performed. The needle was passed with difficulty and with much pain in spite of local anesthesia. Eight days following lumbar puncture, the patient developed typical herpes zoster in the left lumbar area and buttocks, later spreading to the inguinal region and anterior upper third of the thigh. There was severe lumbar pain. Recovery took place in one week following the intravenous administration of sodium iodide and x-ray irradiation from the lumbar puncture site to the twelfth dorsal vertebra. In view of the absent constitutional symptoms and the rapid recovery without antisyphilitic treatment, a neurotropic virus and syphilis were not considered possible etiologic factors and the lesion was assumed to have been due to trauma by the lumbar puncture needle. Judging from the localization of the skin eruption, traumatic irritation must have been transmitted to the first and second lumbar dorsal-root ganglions, resulting in an eruption along the dermatomic distribution of the corresponding nerves.

It has been recognized for many years that attacks of herpes zoster may be precipitated by the administration of arsenic. Four such cases have been reported recently by Knowles and Bolton.²⁹ In one case the zoster developed following the sixth of a series of neoarsphenamine injections. The eruption was distributed over the left arm and disappeared one week following cessation of arsphenamine injections. In the second case zoster appeared on the right upper arm sixty-seven days after the institution of therapy by arsenic trioxide and protiodide of mercury, which were given by mouth in the management of a case of lichen planus. The third patient developed herpes zoster in the left occipital region subsequent to the use of Fowler's solution in the treatment of psoriasis. In the final case, zoster appeared on the right buttock following the twenty-fourth injection of bismuth and Mapharsen in the treatment of syphilis. Knowles and Bolton believe that arsenical herpes zoster is due not to overdosage but to idiosyncrasy.

COMPLICATIONS

As already pointed out, the inflammatory process of herpes zoster may spread from the posterior-horn cells to the anterior-horn cells, with production of motor lesions. Carter and Dunlop¹ discuss in admirable detail the subject of paresis fol-

lowing herpes zoster and report 2 cases. A synopsis of their paper is as follows:

Motor lesions occur infrequently in herpes zoster, although both upper and lower motor neurone palsies have been described. Upper motor neurone lesions were described by Besta and Vercelli (quoted by Rocchi³⁰), Bruce³¹ and Worster-Drought and McMenemy.³² In each of these cases there seemed to be no other explanation for the pyramidal lesions. Among the lower motor neurone palsies the one most often encountered is facial paralysis. Occasional deafness complicating geniculate zoster occurs. The next most frequent palsy appears to be oculomotor paresis complicating trigeminal zoster. Cases of this type have been described by Essén-Möller,³³ Federici,³⁴ Carmody³⁵ and others. Brachial and abdominal palsies are much less common. Lower motor neurone paralysis complicating lumbar or sacral zoster is rare.

Carter and Dunlop have described 2 cases of lumbar zoster, both complicated by lower motor neurone paresis involving the affected segments. These two cases may be summarized as follows:

CASE 1 Two months following an attack of shingles in the right leg, a 73-year-old widow began to feel shaky and complained of neuralgia and weakness of the right leg. Examination revealed recent herpes zoster scars along the distribution of the third and fourth lumbar roots. The right quadriceps was wasted and its power as well as that of the thigh adductors was diminished. All the tendon reflexes were normal except for the right knee jerk which was completely absent. The spinal fluid was normal except for the cell count, which showed 21 cells (20 lymphocytes and 1 polymorphonuclear cell) per cubic millimeter. The patient was treated by a course of irradiation and by exercises of the affected muscles. After 31 months the spinal fluid returned to normal. Nine months following the onset of the eruption the neuralgia was much improved and the quadriceps muscle had returned almost to normal, with only slight persistent weakness. The right knee jerk returned, but was not quite so brisk as the left.

CASE 2 A 53-year-old married woman developed typical herpes zoster on the front of the right thigh and inner aspect of the right leg. The spinal fluid showed increased protein and an increased cell count. Wasting of the quadriceps took place, with almost complete loss of power. The right knee jerk was absent. Complete flaccid paralysis of the quadriceps muscle finally took place and nocturnal neuralgia appeared. After 5 months there was marked improvement, and after 7 months almost complete recovery.

So few cases have been described that it is impossible to determine accurately the course and prognosis of paralyses complicating zoster. Recovery is slow. The increased cell count of the spinal fluid takes weeks to subside. Even after a year the neurologic findings may not reach a normal state.

A case of herpes zoster of special interest on account of the severity and wide distribution of

motor and sensory disturbances has been reported by Abercrombie.³ The patient, a man of sixty-eight, developed pain in the neighborhood of the left hip and thigh and the outer aspect of the left leg. This was accompanied by an eruption of herpetic vesicles on the left buttock and a foot drop on the left side. The herpetic eruption ran its usual course. The pain was troublesome for two months but disappeared in large part after three months. Four months following the onset of herpes zoster, a neurologic examination disclosed a generalized wasting of moderate degree of all the muscles of the left thigh and leg and extreme atrophy of the anterior tibial group. The tibialis anticus, extensor longus digitorum and extensor proprius hallucis muscles were paralyzed, with a reaction of degeneration and resultant complete foot drop. No paresis was observed in other muscle groups. Both knee jerks were active, the left ankle jerk was diminished, and the right ankle jerk even more so, being barely perceptible. Hypoesthesia was present on the outer and anterior aspects of the left leg, and in patches along the anterior and posterior borders of this area. Hypoesthesia of higher grade, involving both pin prick and light touch, was also present on the dorsum of the left foot, extending from the ankle joint to the bases of the toes. There was no disturbance of sensation in the neighborhood of the herpetic vesicles on the left buttock. In March, 1941, one month following the first neurologic examination, a second disclosed evidence of distinct improvement.

Abercrombie in commenting on this case points out that the motor and sensory symptoms did not correspond to the distribution of peripheral nerves, and did not have the character of a root syndrome. The paralysis of the anterior tibial muscles corresponded to a lesion of the fourth and fifth lumbar segments, the sensory changes in the foot to the first and second sacral segments, and the herpetic symptoms to the third sacral segment. Taken together the features were those of a diffuse affection of the cord, almost entirely on the left side, involving both the motor and the sensory regions of the lower lumbar and the upper sacral segments and the root ganglion of the third sacral segment. Such diffuse symptoms are in accordance with the diffuse pathologic changes described by Lhermitte (quoted by Carter and Dunlop¹).

INVOLVEMENT OF SPECIAL ORGANS

Bladder

Herpes zoster of the bladder is a rare syndrome. Rinker³⁶ was able to find only 4 cases in the literature. These cases have been reported by

Dubois,³⁶ Darget,³⁷ Chesterman³⁸ and Eisenstaedt.³⁹ The onset may be characterized by symptoms such as frequency, dysuria and hematuria. Both pus and blood may be found on urinalysis. Cystoscopic examination may show groups of vesicles. These vesicles sometimes ulcerate and may become covered with yellowish or grayish sloughs. They usually heal promptly with or without treatment. Lavages with 0.5 per cent silver nitrate have been recommended. Zoster vesicles may be associated with cutaneous lesions in areas such as the buttocks, or may occur without skin involvement.

Tongue

Herpes zoster of the tongue is an uncommon disease. Two cases have been reported by O'Donnell and Murphy.⁴⁰ One of these was associated with facial herpes. The first case, in a woman of fifty-five, took its onset after exposure to a cold draft. Pain appeared over the right lower jaw and the right side of the mouth. The anterior two thirds of the tongue on the right later developed a purpuric eruption covered with vesicles of pinhead size. Pain in the right ear appeared, followed by deafness. The illness had a profound constitutional effect and the patient remained in bed for a month. The second patient was a man of twenty-six. The onset took place following a cold and a typical vesicular herpetic eruption appeared on the right cheek and chin. In association with this the right anterior two thirds of the tongue showed numerous superficial ulcers, presumably ruptured vesicles. There was easily controlled pain in the right ear but no deafness. A calamine-ichthyol lotion was used on the face and permanganate mouthwashes for the tongue. Complete recovery took place in one month.

Geniculate Ganglion

The syndrome of herpes zoster oticus with facial paralysis and acoustic symptoms was first elaborated by Hunt⁴¹ in 1907. During the thirty-five years since he crystallized medical thought concerning this syndrome, few cases have been reported, and little has been added to Hunt's original concept of the disease. He looked on herpes zoster of the face and neck as due to involvement of ganglions containing the posterior-spinal or unipolar type of cell. These cells are found in the posterior roots of the spinal cord as well as in the gasserian and geniculate ganglions. The geniculate ganglion, though located on a motor nerve, is sensory in type, having unipolar cells, and consequently is the homologue of the spinal and gasserian ganglions. With its afferent fibers, the pars intermedia of Wrisberg, and its efferent fibers, the petrosal nerves, it forms the sensory system of the

facial nerve. Zoster of any zone signifies not only infection of the particular ganglion supplying this zone but also possible spread to neighboring nerves and ganglions. Geniculate herpes zoster, for example, may be associated with pain or zoster in the throat.

Hunt⁴² divided geniculate herpes zoster into four main groups in accordance with severity and extent as follows: simple zoster of the external ear; simple zoster with facial palsy; simple zoster with facial palsy, accompanied by mild disturbance of the acoustic apparatus, such as diminished hearing with or without tinnitus; and simple zoster with facial palsy, together with a Ménière-like complex made up of signs and symptoms such as deafness, tinnitus, vertigo, nystagmus and nausea.

Anstie⁴³ in England was the first physician to report personal observations on his own subjective experiences while suffering from an attack of zoster oticus. More recently Rosenberger⁴⁴ has described his subjective experiences during an attack of zoster oticus with facial paralysis and acoustic symptoms. Both Anstie, in 1871, and Rosenberger, in 1941, misconstrued their initial symptoms, each thinking that he was developing an abscessed ear following exposure to cold. Rosenberger reports daily observations on his vestibular and auditory experiences and the associated facial paralysis. His account is well worth reading. He points out that it is probable that in many cases less severe attacks of zoster oticus manifesting only otalgia or zoster are mistakenly attributed to other causes.

ZOSTER AND VARICELLA

It is now a generally accepted opinion that herpes zoster is a transmissible disease due to a filterable virus. Small epidemics have been known to occur and are said by Sutton¹⁶ to be common. Since 1888 when Bokay suggested the possibility of a relation between herpes zoster and chicken pox, numerous examples of their association in the same family have been reported. The usual circumstances are that in a given family or closely associated group of people some children are exposed to an adult with herpes zoster. After an incubation period of fourteen to sixteen days these children come down with typical varicella without having had any known exposure to chicken pox. Epidemiologic studies of this nature have furnished substantial evidence that chicken pox may appear among persons exposed to cases of herpes zoster.^{9, 45} Likewise, zoster may appear among persons exposed to chicken pox. The usual clinical observations are that, when exposed to adults with zoster, children may develop chicken

pox; and that, when exposed to children with chicken pox, adults may develop zoster. Kundratitz⁴⁶ and later Bruusgaard⁴¹ were able to produce local and general eruptions indistinguishable from chicken pox in children by inoculating them with the fluid from zoster vesicles. Wise and Sulzberger⁴⁷ consider that zoster may be a relatively immune or allergic form of chicken pox, which occurs in those who have had previous acquaintance with the virus in the form of clinical or subclinical chicken pox. This theory would explain why as a rule herpes zoster is rare in children, chicken pox is rare in adults, inoculation of the virus from a case of chicken pox produces chicken pox in children and zoster in adults, and the zoster vesicle virus produces chicken pox in children and zoster in adults.⁴⁷

PATHOLOGY

Carter and Dunlop¹ point out that the pathology of herpes zoster is still somewhat obscure since so few cases come to autopsy. Head and Campbell⁷ in 1900 mentioned that von Bärensprung in 1861 first showed that zoster was a disease of the nervous system associated with changes in the posterior-root ganglions. They described their post-mortem findings in 21 cases in which death occurred at all stages of the disease from three days to over two years after the outbreak of the eruption, and concluded that the primary lesion was an acute round-cell infiltration with areas of hemorrhage in the affected posterior-root ganglions, and that changes found in the posterior-nerve roots and spinal cord were secondary degenerative processes. Price⁴⁸ in 1937 gave a similar account of the pathology of zoster without mentioning the existence of any spinal-cord lesions.

Such views of the pathology of herpes zoster have been challenged by the French school, notably by Lhermitte and his collaborators, who in three communications reported acute inflammatory changes not only in the ganglions but also in the posterior roots, the meninges and the cord itself. In their first case, Lhermitte and Nicholas² described the post-mortem findings in a patient dying seven weeks after the onset of the herpetic eruption. They found perivascular infiltration of leukocytes and mononuclear cells, with vascular dilatation and demyelination in the posterior horns of the affected segments. The anterior horns showed atrophic changes in the cells, with demyelination of the nerve roots and some lymphocytic infiltration, in spite of which no paralysis was observed clinically. There were no changes in the white matter except for one area in the pyramidal tract in which perivascular cuffing was observed. This case showed a pleocytosis of 88

lymphocytes per cubic millimeter on the second day of the eruption. Similar observations were recorded in two subsequent papers (Faure-Beaulieu and Lhermitte⁴⁹ and Lhermitte and Vermès.⁵⁰ In the former, lesions spreading to neighboring segments were found in the posterior horns. Wilson⁵¹ records similar findings by Nicolesco, Thomas and Lamière and by Schlesinger. The view that infection involves the meninges and cord as well as the posterior root and its ganglion is supported by the frequent occurrence, according to Wilson, of a pleocytosis in the cerebrospinal fluid.

TREATMENT

In the management of a case of herpes zoster much can be accomplished by skillful topical applications to the skin lesions themselves. The purposes of this aspect of therapy are to protect the affected parts from irritation, friction and infection. In consideration of the evidence that the virus of zoster is present in the vesicular fluid, the use of local applications takes on an aspect of increased importance in light of the possibility that such applications might also be effective in destroying the causative organisms contained in the skin lesions.

A simple calamine lotion with phenol may be applied as a constant application to the lesions and seems to serve admirably as a soothing wash and as a means of preventing bacterial invasion of the vesicles. Vesicles so treated will usually involute at a satisfactory rate of speed, leaving no scars. The use of flexible collodion with or without antiseptic admixture may be employed as a paint or spray and has been a rather popular remedy, which also prevents secondary infection. It serves as a protective coating to lessen local irritation of the inflamed skin and may, in this way, curb the reflex arc of pain and hyperesthesia. Thick cotton pads are useful in a similar manner and seem to cut off cutaneous stimuli that would tend to aggravate hyperesthesia and pain. Dusting powders and melted paraffin are also beneficial as protective coatings to lessen local irritability and to prevent infection. Most of these topical remedies are very drying and are of chief advantage during the active vesicular stage of the disease. As the vesicles disappear and healthy, non-infected dry crusts form, it is profitable to apply boric ointment or any good ointment base such as lanolin or vaseline in order to hasten involution of the affected areas.

In many cases local therapy may be all that is needed to control discomfort. Sometimes, however, it is necessary to prescribe salicylates, phenacetin, barbiturates, codein or morphine in addi-

tion to local measures. An ethyl chloride spray over the affected dorsal-root ganglions has been found to be helpful in reducing pain. Cobra venom has been employed with prompt, complete and gratifying relief. Local anesthesia, nerve block and subcutaneous injection of thiamin chloride have been recommended as valuable pain-controlling measures. Radiant heat is comforting.

Unfiltered roentgen irradiation of the skin lesions and filtered x-ray therapy to the affected dorsal-root ganglions have been found to be valuable treatments not only in the relief of pain but also in shortening the course of the disease. X-ray used in this way has been recommended in recent treatises by leading authorities such as Pillsbury⁵² and Sulzberger.¹⁴ Keichline⁵³ in 1934 treated 62 cases of zoster with x-ray to the area of the eruption and to the corresponding dorsal-root ganglions, using 148 r through a 3-mm. aluminum filter at a distance of 30 cm. Ninety per cent of these patients were relieved by one dose; the others required one or two additional exposures.

Ordinary uncomplicated shingles requires little or no treatment and does not interfere with the patient's activities. Some patients, however, run a protracted and stormy course with considerable pain that is difficult to control. They require the utmost skill in management and test to the limit the physician's therapeutic legerdemain. In handling these cases it is well for the physician to be supported by a fairly complete knowledge of the modern therapeutic armamentarium pertaining to zoster. Many bizarre empirical treatments have been described, and although it is difficult to understand the manner in which they act, it is well to know about them.

Posterior-pituitary extract has been recommended by Sidlick⁵⁴ and others,⁵⁵ not only as a means of relieving pain but as a measure effective in shortening the course of the disease. Obstetric pituitrin may be administered by the subcutaneous route in doses of 0.5 to 1 cc. daily. Pituitrin is contraindicated in the presence of hypertension, coronary disease, myocardial disease and pregnancy, and it is perhaps better not to use it in elderly people even in the absence of these conditions. Portnoy⁵⁶ employed surgical pituitrin in 1 cc. doses daily by the subcutaneous route, and reported prompt relief from pain in patients whose discomfort had not been relieved by local applications, infrared heat, sodium iodide and morphine. Sulzberger and Wolf¹⁴ recommend obstetric pituitrin in daily doses of 0.5 to 1.0 cc. for three to five days, and consider it to be the most effective form of treatment now in use. Goodman and Gilman,⁵⁷ on the other hand, state

that the mechanism of action of pituitrin "is obscure and the clinical evidence of its value is contradictory."

The intravenous use of sodium iodide has been recommended by Ruggles⁵⁸ and others. Tobias⁵⁹ considers it the treatment of choice because of its effectiveness and dependability. Sulzberger and Wolf¹⁴ consider this to be one of the two best modern forms of treatment, but warn against iodine intoxication, iodine allergy and iododerma. Ruggles advises the intravenous injection of sodium iodide in 2-gm. doses (10 cc. of a 20 per cent solution), to be given on the first, second, fourth and seventh days.

In the resistant ophthalmic type of zoster, diphtheria antitoxin has been recommended.⁶¹ It may be given in doses of 5000 units, repeated two days later if necessary. Autohemotherapy has been in vogue for many years in the treatment of zoster. It may be given merely by removing 5 to 10 cc. of whole blood from the antecubital vein and injecting it into the gluteal region every day or two.

Cobra venom has been used extensively for the relief of pain in cancer, tabes dorsalis, Parkinson's disease⁶⁰ and painful x-ray burns.⁶¹ During the last several years a sterile saline solution of cobra venom has been used for the relief of pain by investigators in France, India, Argentina and the United States.⁶²⁻⁷⁰ Of these, Macht⁶⁷ in the United States reported 6 zoster patients who obtained striking relief. Three investigators in Italy⁷¹ employed cobra venom successfully to relieve the pain of herpes zoster. McDowell⁷² has reported its use in 6 cases, with prompt and complete relief. Both Macht and McDowell found that the pain of zoster responds much more promptly to cobra venom than it does in other conditions. No reactions either local or general were observed. No depressive reactions occurred. Very few reactions have been reported in the literature and the margin of safety seems high. For psychologic reasons it is advisable not to reveal to the patient the nature of the injections; Black⁷³ observed vomiting and dizziness when the patients knew the nature of the remedy, and proved conclusively that these symptoms were of psychologic origin.

Rosenak⁷⁴ reported relief from pain and regression of vesicles in zoster after intravertebral and paravertebral injections of 0.5 per cent aqueous procaine solution. Hollander⁷⁵ showed that an oil-soluble anesthetic could be injected subcutaneously into the hyperalgesic areas of zoster with prompt relief of pain, and without recurrence when the anesthesia wore off four weeks later. Secunda, Wolf and Price⁷⁶ used the method of Hollander in the treatment of 15 cases of herpes zoster, selected at random. They employed 0.5 to

2.0 per cent novocain and three preparations of anesthetic oil including Nupercain-Ciba, Hollander's formula and a modification of Hollander's formula containing benzocaine, benzyl alcohol, phenol and oil of sweet almond. The areas of hyperesthesia were mapped out by the usual methods, such as pinprick, brush and pinching. These areas were cleansed with alcohol and infiltrated subcutaneously to the point of total anesthesia. No nerve block was induced and anesthesia was confined to the area injected. Anesthesia from the novocain solution lasted one to two hours and that from the oil solution for about a week. Fourteen patients were injected with an aqueous solution of novocain and complete relief from pain ensued immediately in 13, lasting one to thirty or more hours, after which pain recurred with equal or greater severity in all but 4 patients. In 1 case the pain was made worse by the injection. Eight of the 14 patients and 1 other were subsequently treated by the injection of anesthetic oil. Complete relief of pain took place in 7 of these 9 cases. Local reactions to the anesthetic oil injections included soreness, redness, swelling and pain at the site of injection.

Relief from the acute attack was experienced by 13 of the 15 patients. Ten of these 13 were permanently relieved of all discomfort. The clinical course of the skin lesions was, however, not affected and regression of the vesicles occurred in the expected seven to fourteen days.⁷⁷ Two cases of classic post-herpetic neuralgia failed to respond to this method of treatment. Relief of pain in this series of cases was accompanied by amelioration of muscular disabilities, improved appetite, normal sleep and accelerated return to work.

The use of vitamin B₁ (thiamin chloride) in the treatment of herpes zoster is a subject of considerable general clinical interest. The fact that zoster has been reported to occur as an apparent complication of the administration of large doses of vitamin B₁ does not exclude the possibility that, in small doses, this vitamin may be of value in treating this disease. The fact that zoster occurs as a complication of the administration of large amounts of thiamin chloride provides evidence that this vitamin may have a selective action on the dorsal-root ganglions and that, in properly regulated dosage, it may be of therapeutic usefulness.

Steinberg⁷⁸ reported 3 cases of typical herpes zoster occurring as an apparent complication of the administration of a large dosage of vitamin B₁. In 1 of these cases the author was able to produce zoster on two occasions by this procedure. The other 2 patients refused further treatment on account of the zoster pain that they suffered while taking the thiamin chloride.

The case in which two attacks of zoster were produced was of special interest. The patient was a white woman of fifty-one, who was being treated for typical atrophic arthritis of twenty-six years' duration. She was given 800 units of vitamin B₁ by mouth daily and 2000 units by injection weekly. In the fourth week of this plan of treatment, typical herpes zoster developed and persisted for five weeks in spite of immediate cessation of vitamin B₁ therapy. Six weeks later the same dosage of vitamin B₁ was given again, and after the same four weeks' interval, a second typical attack of herpes zoster developed and again persisted for four weeks in spite of immediate cessation of therapy. This case is all the more remarkable because of the fact that second attacks of zoster are so exceedingly rare. Perhaps the zoster in this case was actually produced by a thiamin chloride effect on the dorsal-root ganglions and not by lowering the resistance of these ganglions to invasion by the varicella virus. Steinberg concluded that large doses of vitamin B₁ are capable of irritating peripheral-nerve plates.

The known value of thiamin chloride in the treatment of neuritis and its influence in preventing certain degenerative nerve diseases led Goodman⁷⁹ to use this vitamin in the treatment of herpes zoster. He reasoned that since the pain of zoster is due to an inflammatory process in the posterior nerve roots and to degenerative processes in the peripheral nerve tracts, perhaps thiamin chloride might be an effective form of therapy. He administered it in a series of 5 cases and obtained gratifying results in all of them. These cases were treated locally by applications of Merthiolate in collodion. Thiamin chloride was administered subcutaneously in dosage of 3000 units at varying intervals and for a varying series of injections, usually six to ten. The results were far better than those obtainable by routine local applications and salicylates. The pain was relieved more promptly and the lesions cleared at an earlier date. Total disability was noticeably decreased, and in all respects the results seemed sufficiently good to justify further investigation.

Rattner and Roll⁸⁰ used crystalline thiamin in doses of 2000 international units subcutaneously every second or third day in a series of 16 cases of herpes zoster. Seven of the patients were males and 9 were females. Two children, aged nine and thirteen, were completely relieved of symptoms after the first injection; they were treated on the third and seventh days of the disease, respectively. A third child treated on the seventh day of the disease showed no striking effect and the disease ran its usual mild course. One patient aged sixty-two obtained considerable relief following the subcutaneous injection of 6000

units on the fifth day of the disease. Another patient aged forty-eight obtained much relief after receiving 8000 units on the fifth day. In the remaining 11 cases, including 2 cases of severe post-herpetic pain, no favorable effects whatsoever were observed. The average total dose of thiamin chloride used in this series was 5620 international units. Rattner and Roll considered their results disappointing, perhaps because the patients were mostly in the older age group and perhaps because treatment may have been begun too late. Their results were quite different from the gratifying ones reported by Goodman. It may be observed that the latter used thiamin chloride in much larger total doses and by a much more persistent type of therapy.

Gordon⁸¹ used thiamin chloride by mouth in the rather conservative dosage of 3 to 10 mg. daily in a series of 6 obstinate cases of herpes zoster of two to five months' duration. The suffering was so great in 2 cases that the patients made several attempts at suicide; all lost appetite and weight and had a reduction of hemoglobin. In all cases the zoster was thoracic in location, corresponding to the distribution of the third to twelfth spinal segments, involving in each case two or three segments of the spinal cord. Neurologic changes, such as abolition of the patellar and Achilles reflexes, anesthesia, hypesthesia and hyperesthesia, were present in some cases. Gordon found in the treatment of these rather severe cases that vitamin B₁ alone was no more effective than the customary standard forms of treatment. He found, however, that when he combined vitamin B₁ with sedatives, local applications containing cocaine or procaine, applications of heat and cold and autohemotherapy, he was able to produce striking improvement of the pain and skin lesions.

In the papers of Gordon and of Rattner and Roll may be found extensive reviews of the literature on the use of thiamin chloride in the treatment of numerous and varied diseases, including neuritis, sciatica, general debility, inflammatory and degenerative diseases of the central nervous system, multiple sclerosis, degeneration of the pyramidal tracts, beriberi, pruritus ani, pruritus vulvae, inoperable cancer, diabetic polyneuritis, alcoholic neuritis, colitis, irradiation illness and acrodynia in children. These reports, all written in a rather optimistic vein, made it seem rational to use thiamin chloride in the treatment of zoster.

Smith⁸² has given a helpful analysis of the extensive literature on the treatment of herpes zoster, and has reported the excellent results that he obtained by the extraordinary procedure of injecting thiamin chloride into and beneath the skin of

areas involved in the skin eruption of herpes zoster. Three patients were treated by this method and all obtained prompt and remarkable relief. Only relatively small areas were treated, and therefore it seemed unlikely that a purely local effect on nerve endings could explain the results. Smith considered that absorption along the lymphatics might bring about a high concentration of thiamin chloride in the region of the affected dorsal-root ganglions. He used a combination of intra-dermal and subcutaneous injections of thiamin chloride daily for a series of three or four injections. Striking relief of discomfort usually took place within a few hours following the first injection. Complete and permanent relief ensued after the third or fourth injection.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29181

PRESENTATION OF CASE

A fifty-eight-year-old physician entered the hospital because of intermittent attacks of low-back pain.

Eleven years prior to admission, after a strenuous day of ice skating, the patient developed severe localized low-back pain that interfered with his activities for three days but did not confine him to bed. Six years later a similar attack of pain occurred after ice skating and lasted three days. During these episodes he was unable to dress without assistance or bend forward because of the pain, and once, while shaving, his legs gave way and he fell to his knees, but soon recovered. Five or six times during the next four years he was awakened from a sound sleep by severe "gripping" pain that seemed to be just above the rectum and was relieved by warm-water enemas. Five months before entry the patient developed a feeling of tension in the posterior thigh muscles. Two weeks before admission, steady, sharp pain developed in the region of the lower lumbar spines that radiated down the posterior aspects of both thighs to the knees and bilaterally to the inguinal regions and scrotum. The lower-lumbar and posterior-thigh pain was intensified by coughing, sneezing or straining at stool. When sitting, "pins and needles" developed in the pressure areas of the buttocks. One week before entry the patient noticed numbness on the outer aspect of the left foot, which seemed to disappear after a night's rest. Five days before admission, while applying a cast, excruciating pain started in the lower lumbar region and radiated down the posterior aspects of both legs to the heels. There was a sensation of numbness and of "pins and needles" in both feet, and the patient was unable to walk. After forty minutes' rest the pain gradually subsided. During the night he was awakened by a similar attack, which required morphine for relief. Nine hours later he found that he was unable to void and had developed anesthesia involving the penis, scrotum, perineum and perianal region. During the next day the anesthesia diminished rapidly in intensity but the patient had to be catheterized. After that he was able to void

spontaneously. His bowels had not moved for five days, although he had previously been regular. Adhesive-tape leg traction was applied at a community hospital, after which the patient was quite comfortable. A lumbar puncture demonstrated complete block and yielded only a few cubic centimeters of yellow fluid, which had a protein content of 750 mg. per 100 cc. The exact location of this puncture was not known.

Physical examination revealed a well-developed and well-nourished man lying comfortably in bed. The heart, lungs and abdomen were normal. There was weakness of dorsiflexion of the right foot and great toe. The strength of the other muscle groups on this side could not be determined because of the interfering pain in the lumbar region, but a full range of motion seemed present except for straight leg raising, which was limited on the right to 45° and on the left to 30° by sharp pain in the posterior aspect of the thigh and legs. There was slight tenderness to the right of the fourth and fifth lumbar spinous processes. The knee jerks were present and equal. The ankle jerk was absent on the right, but normal on the left. There was impairment of all forms of sensibility over the medial parts of the buttocks, in the perineum and over the lateral half of the leg, dorsum and sole of the foot on the right, with marked subjective numbness of the third, fourth and fifth toes bilaterally, which was more noticeable on the right. The neurologic examination was otherwise not remarkable. The patient reported loss of sphincter sensation during defecation.

The blood pressure was 155 systolic, 85 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 5,900,000, with a photo-electric hemoglobin of 16.6 gm. per 100 cc., and a white-cell count of 6600, with 68 per cent neutrophils, 16 per cent lymphocytes, 11 per cent monocytes, 3 per cent eosinophils and 2 per cent basophils. The urine was acid and had a specific gravity of 1.020, and the sediment contained 2 red cells and 5 white cells per high-power field. A blood Hinton test was negative. A lumbar puncture in the interspace between the first and the second lumbar vertebra revealed normal dynamics. The fluid was slightly xanthochromic, with a protein of 266 mg. per 100 cc. and was otherwise negative.

A roentgenogram of the chest was normal. X-ray films of the spine and pelvis disclosed calcified deposits along the anterior margins of the spine in the region of the interspinous ligaments. In the lower dorsal and upper lumbar regions there were small spurs on the anterior margin of the bodies of the vertebrae. The intervertebral

spaces were not narrowed or deformed. There were no localized widenings of the neural canals or erosion of the lateral masses. Injection of iodized oil revealed a block at the level of the fourth lumbar disk (Fig 1). There was a round



FIGURE 1 Iodized Oil Arrested above the Fourth Lumbar Intervertebral Disk

ed filling defect above the inferior margin of the lamina. The nerve roots were displaced medially, and the defect was more pronounced anteriorly and on the right side.

An operation was performed on the fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR JOST MICHELSEN: After reading this story one can reach a preliminary conclusion that ought to prove correct. This patient had a surgical lesion in the lower lumbar spine. We may further assume that the surgeon expected to find a herniation of the nucleus pulposus at the fourth lumbar interspace and that he also was prepared to open the dura and explore the cauda equina if no extradural lesion was found.

The indications for surgical exploration are obvious: there was a block on lipiodol examination, there was also dynamic block, with a protein of

50 mg per 100 cc, below the lesion, the dynamics were normal above the lesion, where the protein was lower but still abnormally high.

Exaggeration of pain on coughing, sneezing and straining is further evidence of a space limiting lesion in the spinal canal, which, however, is of minor significance in view of the lumbar puncture and lipiodol findings.

We also know that the upper level of this lesion was at the fourth lumbar disk and that the mass producing the defect was anterior and on the right side. The defect was rounded, and apparently there was no cup formation, which is characteristic of an intradural lesion. All these observations are suggestive of a large herniation of the nucleus pulposus. So are the history and findings, although they do not correspond entirely with those observed in the average case. Consistent are the long story with intermittence of symptoms, the limitation of forward bending, and the fact that the low back pain—the only symptom for years—preceded the onset of radiating pain in the lower extremities and the other symptoms which will be discussed later. Perhaps it is also significant that the two first attacks of back pain started after ice skating.

The distribution of the nocturnal pruns just above the rectum is uncommon, and I also do not quite understand how they were relieved by warm water enemas, whatever their nature might have been. Fortunately the sharp pruns developing two weeks before entry were again in a more appropriate place, but it should also be noted that there was radiation of this pain down the posterior aspects of both legs and to both inguinal regions as well as to the scrotum. Pain in the inguinal region from a lesion whose upper level has been demonstrated to be at the fourth lumbar disk must be referred pain. Subjective sensory disorders at segments higher than the actual lesion have been observed in ruptured disks of the lumbar as well as the cervical spine, one wonders if perhaps they are due to the peculiar setup of the lumbar and brachial plexuses.

An outstanding feature of these sharp excruciating pruns is their bilateral involvement of the lower extremities. The bilateralness is further emphasized by paresthesias in both feet, weakness of the bladder and bowel, and sensory disturbances in the saddle area. The findings on examination are in close agreement with these symptoms. There was saddle anesthesia for all forms of sensation, that is, in the area supplied by the third to fifth sacral segments, as well as numbness of the third, fourth and fifth toes bilaterally, or in the first and second sacral dermatomes. On the right leg the anesthesia apparently had a first and second sacral distribution. Also recorded is weakness of the anterior tibialis and extensor hal-

lucis longus muscles, disclosing disease of the fifth lumbar and first sacral anterior roots. In other words, the posterior roots of the cauda equina from the fifth lumbar to the fifth sacral on both sides and the fifth lumbar and first sacral anterior roots on the right were damaged.

It is known that a large herniation of a nucleus pulposus can produce the symptoms that this patient had, although the commoner syndrome consists of low-back pain, tenderness of the lower lumbar spaces, sciatic pain on one side, well-localized paresthesia and hypesthesia, limitation of straight leg raising, diminution of the ankle jerk, increased protein in the cerebrospinal fluid, a lipiodol defect and intermittence and recurrence of symptoms and signs.

I therefore come to the conclusion that the surgeon found a large herniation of the fourth lumbar disk on the right side extending far toward and beyond the midline. This is the commonest extradural lesion in the lumbar area, and there is no evidence, so far as I can see, to indicate any other type of extradural lesion. I consider the possibility of an intradural mass as remote in view of the course of the disease.

DR. RICHARD SCHIATZKI: The lumbar spine shows no evidence of disease, as stated in the report, aside from minor degenerative changes. Lipiodol shows a complete block just above the lower edge of the fourth lumbar vertebra. The lipiodol runs down to that point and stops there. A little lipiodol runs out into the nerve sheaths.

You can see that the defect is larger on the right side than on the left, but complete block is present. The lateral view shows that the defect is definitely larger anteriorly. There is not the real cap formation that one usually sees in patients with a well-rounded tumor in this area, such as a neurofibroma. In any tumor, whether intradural or extradural, its smooth surface is demonstrated by the lipiodol, and is usually more symmetrical with an intradural tumor than with an extradural one.

Do you want me to go beyond that?

DR. CHARLES S. KUBIK: Have you a film more characteristic of ruptured disk?

DR. SCHIATZKI: Arrest of the lipiodol is by no means the usual finding in cases of ruptured disk. Here, in another case, you see the characteristic appearance of the lipiodol. This patient had a rupture of the fourth disk on the left side, which produced a well-localized defect of the lipiodol column of the fourth disk that, as Hampton and Robinson^{*} reported, is of the shape of an anvil or half an anvil, with the defect on the medial surfaces.

DR. SCHIATZKI: Is it interesting that

*H. J. Hampton and Robinson, "The appearance of the lipiodol column after injection of lipiodol in cases of ruptured disk with specific back pain,"

White demonstration after injection of lipiodol, accompanied by low dose. 36 782-803, 1936.

the patient in the present case had a referred type of sensory disturbance well above the involved area. This was largely a paresthesia, which does happen.

DR. W. JASON MIXTER: Pain in the groins is not too uncommon. You see that every once in a while with a lesion of the fourth or fifth lumbar disk.

CLINICAL DIAGNOSIS

Ruptured intervertebral disk (fourth lumbar), with compression of nerve roots.

DR. MICHELSEN'S DIAGNOSIS

Ruptured intervertebral disk (fourth lumbar).

ANATOMICAL DIAGNOSIS

Ruptured intervertebral disk (fourth lumbar).

PATHOLOGICAL DISCUSSION

DR. KUBIK: A large protrusion of the nucleus pulposus of the fourth lumbar disk on the right side was found at operation. The spine was not fused. Three months later the patient was back at work, taking care of a busy practice.

CASE 29182

PRESENTATION OF CASE

A sixty-four-year-old salesman entered the hospital because of weakness, fainting spells and tarry stools.

The patient apparently was quite well until nine months before admission when at a community hospital a transurethral resection of the prostate was performed because of frequency, urgency, nocturia and a high bladder residual. Soon after leaving the hospital he frequently noticed that his stools were tarry. Three months before entry the patient suddenly felt weak, cold and sweaty and fainted. He recovered after several minutes, but felt exceedingly weak for a day. Because he could not carry on his daily duties, he took a vacation. A month before admission he had several similar fainting spells but quickly recovered consciousness spontaneously. Several hours later he usually passed a semiliquid stool that resembled "coffee-grounds." His physician prescribed bed rest and an ulcer diet amplified with iron, but this failed to relieve the persistent weakness and easy fatigability. There was no nausea, vomiting, pain, constipation, jaundice or persistent diarrhea. The patient had lost 10 pounds during the period of illness.

The family and past histories were noncontributory.

Physical examination disclosed a pale, tired-looking man who lay quietly in bed. A soft systolic murmur was audible over the entire precordium. The lungs and abdomen were normal. The blood pressure was 118 systolic, 70 diastolic.

tolic. The temperature, pulse and respirations were normal.

The red-cell count was 3,870,000, with a photoelectric hemoglobin of 9.5 gm. per 100 cc., and the white-cell count 11,200. The urine was negative. A blood Hinton test was negative. The nonprotein nitrogen was 24 mg., and the protein 6.3 gm. per 100 cc.; the chloride was 97.6 milliequiv. per liter. The prothrombin time was 21 seconds (normal, 16 seconds).

A barium meal showed curling in the lower half of the esophagus. There was a slight hiatus hernia. The stomach showed a filling defect, measuring 6.0 by 4.3 cm., on the anterior wall in the region of the angulus and lying toward the lesser curvature. This was clearly visible only with the patient lying prone. The lesion had a broad shape and extended upward to the level of the esophageal hiatus but lay anterior to it and had a lobulated surface. There was an ulceration on the lesser curvature, and in the films brought in by the patient the filling defect appeared to extend upward to the region of the cardia. The mucosa on the posterior wall of the stomach appeared normal. The duodenum and proximal jejunum were normal.

A roentgenogram of the chest showed no definite evidence of metastases. There was some increased density in the right second interspace consistent with old infection. The apex of the heart was somewhat rounded, and the aorta was slightly tortuous.

On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN, JR.: This case resolves itself into the discussion of tumors of the stomach, and in large part the answer should be given by the x-ray men. I might say that I do not know anything about the x-ray interpretation of tumors of the stomach.

We may also consider the case from a statistical point of view. Of roughly 5000 surgical specimens of stomachs resected during a period of years at the Mayo Clinic,* about 2300, or nearly half, were cancers; about half that number were peptic ulcers; lymphosarcomas numbered 35; there were 12 fibrosarcomas or leiomyosarcomas, 2 angiosarcomas, and 4 cases of tuberculosis, with no cases of syphilis. Considering the present case from more than a statistical or an x-ray standpoint does not seem to be possible.

The predominant feature of the history of this man was bleeding. Of the lesions in the stomach that are more prone to bleed than others I should think lymphosarcoma was probably as promi-

nent as any. The x-ray appearance described as a lobulated surface does not seem applicable to carcinoma.

This might be a good time to look at the x-ray films, except that I do not see how I can get any more information without asking direct leading questions.

DR. RICHARD SCHATZKI: I do not know the answer, so you may question me all you wish.

These are the films brought in from the outside. They show this large filling defect (Fig. 1). The lower edge is clearly indicated about 7 cm. proximal to the pylorus, and is markedly lobulated. There is also a deep, rather linear, crater somewhere near the center of the defect. The upper edge is not so clearly visible, but I doubt if it goes to the cardia. These are the films taken here. You see in the big films the same appearance that was seen on the outside films, except that the crater is not filled so much.

DR. HAMLIN: These films certainly are not spectacular.

DR. SCHATZKI: Here are two spot films. The lobulation on one of them is by no means so striking as that on the big films, and I am inclined to think that that is of some significance.

DR. HAMLIN: One thing that I do remember about x-ray interpretation of tumors of the stomach, which may not be of significance here, is that some leiomyomas of the stomach have a very characteristic picture, which resembles in outline that of the human cervix. Purely on that basis, although I have no business making an interpretation on x-ray evidence, I will make leiomyoma or leiomyosarcoma my first choice.

DR. SCHATZKI: The differential diagnosis of a case like this lies between the three tumors that Dr. Hamlin has mentioned. Lymphoma is the least likely and the argument usually centers around a spindle-cell tumor or just another cancer, and at times it is impossible to make a differential diagnosis, since carcinoma may imitate the x-ray appearance of a spindle-cell sarcoma. The central ulceration that is typical of a sarcoma may be just a cleft in the cancer that has filled with barium. On the other hand, this sharp edge is very unusual in cancer. It occurs occasionally if there is a dish-like cancer that has an elevated "life-saver" rim with a smooth edge. Such a cancer, however, has a large central crater, whereas this is relatively small. I think I shall agree with Dr. Hamlin and call it an intramural spindle-cell tumor that has become ulcerated.

DR. TRACY B. MALLORY: Benign or malignant?

DR. SCHATZKI: It is impossible to say on the x-ray evidence.

DR. MALLORY: This is essentially an x-ray diagnosis. Has Dr. Sosman an opinion?

*Futerman, G. B., and Balfour, D. C. *Stomach and Duodenum*. 958 pp. Philadelphia: W. B. Saunders Company, 1935. P. 73.

DR. MERRILL C. SOSMAN: It is interesting that the films with the patient prone show an irregular lobular outline. The spot film shows a smooth outline when the patient was upright or more

able tumor was found, which was nearly spherical. On palpation of the external surface of the stomach, Dr. A. W. Allen thought it was a spindle-cell tumor. He therefore did a relatively limited gas-



FIGURE 1. *First Film of Stomach Showing Filling Defect with Lobulated Border and Central Crater.*

probably supine. So probably the prone film gives a truer appearance of the edge of the tumor, and working on the same hypothesis or line of reasoning as Dr. Schatzki used, I should say that it fits better with adenocarcinoma and that the cleft or fissure is merely barium that came in between the two lobules of adenocarcinoma. Just to be different, I shall put my money on that horse.

CLINICAL DIAGNOSIS

Leiomyoma of stomach.

DR. HAMLIN'S DIAGNOSIS

Leiomyoma or leiomyosarcoma of stomach.

ANATOMICAL DIAGNOSIS

Fibrosarcoma of stomach.

PATHOLOGICAL DISCUSSION

DR. MALLORY: On exploration a smooth, mov-

tric resection and provided us with this specimen. You can see that the mucosa over the entire tumor is intact except for a small area of ulceration that is hardly more than a dimple on the top of the dome. A fistulous tract only a couple of millimeters in diameter extends downward from the ulcer to a cavity perhaps 2 cm. in diameter that lies deep in the center of the tumor. Obviously barium would have had some difficulty in penetrating to this central cavity.

DR. SCHATZKI: It probably was filled in the outside films but not in the hospital ones.

DR. MALLORY: On microscopic examination the tumor proved to be a fairly rapidly growing, poorly differentiated, spindle-cell sarcoma, which was undoubtedly malignant and probably fibrosarcomatous.

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ANNUAL MEETING

The one hundred and sixty-second anniversary of the Massachusetts Medical Society will be held at the Hotel Statler, Boston, on May 24, 25 and 26, the program of the meeting appears elsewhere in this issue of the *Journal*.

According to the schedule adopted in 1942, the annual meetings of the supervising censors and of the Council will be held in the late afternoon and evening, respectively, of Monday, May 24, the day before the opening of the regular sessions.

The Committee on Arrangements has prepared an extremely timely, interesting and valuable pro-

gram of scientific papers. As would be expected, the majority of these are related, directly or indirectly to the war effort.

The first morning will be devoted to a symposium on burns, with special reference to the Coconut Grove disaster. Following the business portion of the annual meeting of the Society, Dr. Edward P. Bagg, of Holyoke, will deliver the annual oration. The afternoon session largely concerns wartime medical topics, and after the annual dinner that evening, at which the guest speaker will be Mr. James A. Hamilton, president of the American Hospital Association, the Shattuck Lecture will be given by Dr. George W. Thorn, the newly appointed Hersey Professor of the Theory and Practice of Physic at the Harvard Medical School.

The program for the second day covers a miscellaneous group of topics. The following papers should be of particular interest: 'Newer Chemotherapeutic Agents,' by Dr. Charles A. Janeway, 'Meeting Nutritional Requirements in Time of War,' by Dr. Russell M. Wilder, of Washington, D. C., 'Oxygen Therapy and Positive Pressure as Related to Gas Poisoning in War and in Civilian Disorders,' by Dr. Alvin L. Barach, of New York City, and 'Present Day Rapid Methods of Treating Syphilis,' by Dr. Harold N. Cole, of Cleveland. The various sections will hold luncheon meetings, and at each a short talk is scheduled.

The scientific and technical exhibits, although somewhat smaller than they have been in the last few years, will be no less interesting. And, as in previous years, there will be a continuous motion-picture program on both days.

Two of the usual accompanying activities—the ladies' entertainment and the golf tournament—have been canceled, owing to the difficulties of transportation.

The Committee on Arrangements, which is composed of Dr. Gordon M. Morrison, chairman, and Drs. Roy J. Heffernan, Sidney C. Wiggan, Richard I. Smith and G. Guy Bailey, deserves great praise for planning such an attractive program.

at a time when it is difficult to obtain authoritative speakers. This can be evidenced only by a good attendance of the members of the Society, and all are urged to be present.

QUOTAS FOR MEDICAL OFFICERS

TO DETERMINE how many of a given number of medical officers should be obtained from each state and how these needs should be allocated to subdivisions within the state seems to be a simple matter. On the basis of percentages, knowing the total number of men required and the numbers of licensed physicians in the country as a whole, in the state and in the subdivision, figures can be jotted down within a few minutes, particularly if one is adept in the use of a slide rule. But the matter of determining quotas is far more difficult.

Physicians are not divided throughout the country according to population. They tend to congregate in cities, especially large cities, where opportunities are greater than they are in the rural districts. There, modern hospital facilities are available, the need for specialists, including those concerned with industrial medicine, and for instructors and research workers, is great, the chances for the continuous postgraduate education that is so necessary for the successful practice of medicine are excellent, and life, by and large, is relatively easy. As a result the number of physicians per unit population is higher in Massachusetts than in Kansas, and higher in Suffolk County of Massachusetts than in Franklin County. As a corollary it is obvious that to cut the number of physicians in half would create more of hardship on the civilian population in Kansas than it would in Massachusetts, and more in Franklin County than in Suffolk County. Thus, the percentages of physicians from the manufacturing states and from the large cities must be higher than those from

the agricultural states and the rural communities. On the other hand, the strict application of the one-physician-per-fifteen-hundred-inhabitants yardstick to large cities is impracticable, owing to the nature of local medical practice. In addition, it must be acknowledged that, generally speaking, a commission in the Army or Navy offers more financial security to the physician in the country than it does to his counterpart in the city. All these facts—and many more—have been considered by the Directing Board of the Procurement and Assignment Service in Washington and by the state committees of this agency when quotas and allocations were determined.

The total quota for Massachusetts—2400 medical officers—is high on a percentage basis, as are the allocations to the districts comprising Metropolitan Boston. However, in spite of statements to the contrary, the medical profession has responded wholeheartedly to the call, and according to Dr. Reginald Fitz, state chairman of the Procurement and Assignment Service, close to the desired number of men have already been obtained. This does not mean that no more are needed, but it does signify that those physicians who volunteer in the future must, for the most part, come from the urban districts.

MEDICAL EPONYM

VALSALVA MANEUVER

This maneuver was described by Antonio Maria Valsalva (1666–1723) in his book *De Aure Humana Tractatus* [*Treatise on the Human Ear*] (Utrecht, 1717). A portion of the translation from page 84 of a later edition (Leyden, 1735) is as follows:

If a person who has a continuously discharging abscess in or near the eardrum attempts, with his mouth and nostrils closed, to compress the air inside, then, as this is done, the bloody matter usually flows out freely into the auditory meatus.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL HEALTH

OBSTETRIC CASE HISTORY: ACUTE
APPENDICITIS COMPLICATING LABOR

A twenty-four-year-old primipara was first seen when approximately thirty-five weeks pregnant. Her past history was essentially negative. She had had no contagious diseases, nor had she been operated on. Catamenia began at the age of twelve and had always been regular, lasting three days. The early part of the pregnancy was accompanied by a normal amount of morning sickness and some frequency of urination. When about twelve weeks pregnant, she was said to have had an attack of abdominal pain with vomiting. A similar attack occurred two months later. Except for these incidents, the pregnancy had been uneventful.

Physical examination showed a well-developed and well-nourished woman. The heart and lungs were negative. The breasts were consistent with pregnancy. The blood pressure was 120 systolic, 80 diastolic. The uterus was enlarged to the size of a pregnancy of approximately eight months. The fetal heart was heard, and the external pelvic measurements were within normal limits.

Five days after this first office visit, the patient was having a good deal of pain in the upper part of the abdomen. Physical examination revealed no abdominal spasm, and the temperature was normal. This distress was relieved by an enema.

The next evening the membranes ruptured spontaneously, and the patient began to have cramp-like abdominal pains every twenty minutes. Twelve hours later she had a temperature of 100°F., a pulse of 80, and a white-cell count of 17,000. She was definitely in labor. Rectal examination revealed an obliterated cervix and a head that was well descended into the pelvis; the cervix was dilated to admit two fingers. The patient was lying in bed comfortably. Her tongue was dry. The left side of the abdomen was soft, but the right side was tender and spastic. This tenderness did not extend into the pelvis. A catheter specimen of urine showed no evidence of pyelitis. The elevated white-cell count, the moderate rise in temperature and the rigidity and tenderness of the abdomen pointed to an acute abdominal condition, the most likely diagnosis be-

ing acute appendicitis. A surgical consultant confirmed the diagnosis of an acute condition of the abdomen, and an obstetric consultant advised immediate operation.

Under spinal anesthesia the abdomen was opened by a right paramedian incision. Free purulent fluid was found in the right lower quadrant. The appendix, which was lying behind the uterus, covered with a layer of fibrin and pus exuding from its tip, was removed. The stump was not inverted. Ten grams of sulfanilamide was put in the abdominal cavity, and the abdominal wall was closed in layers, with a drain to the site of the appendix.

Labor proceeded during the day, and a simple forceps delivery was accomplished about ten hours after the operation. Spinal anesthesia was again used. The baby cried lustily. It weighed 5 pounds, 9 ounces, at birth and was discharged well from the hospital.

For the first three days the patient's convalescence was accompanied by a temperature ranging from 98 to 101°F. and a pulse varying from 100 to 120. There was no postoperative vomiting, and little distention. Nine days after the operation the patient complained of pain in the right shoulder. The temperature rose to 100°F., and the white-cell count was 9000; x-ray examination showed an infarct in the right lung. The temperature remained elevated for forty-eight hours, but there was no cough. The drain and stitches were removed on the thirteenth postoperative day. Subsequent convalescence was uneventful.

The pathological report was "acute appendicitis."

Comment. This case illustrates the intelligent handling of acute appendicitis during labor, which is relatively uncommon. If operation had been delayed until after the baby had been delivered, it is quite likely that a fatal peritonitis would have developed. When this case was seen, it was evident that an acute condition of the abdomen existed. Pyelitis was eliminated by negative urinary findings. A pedunculated fibroid and an ovarian cyst with a twisted pedicle were considered, but no definite tumor could be demonstrated. Hence, the diagnosis of appendicitis seemed to be the logical one.

Any acute abdominal condition during pregnancy demands surgery, and the sooner the operation is performed, the better the chance for recovery, even if the patient is in labor.

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PROGRAM OF THE ONE HUNDRED AND SIXTY-SECOND ANNIVERSARY OF THE MASSACHUSETTS MEDICAL SOCIETY

Monday, Tuesday and Wednesday, May 24, 25 and 26, Hotel Statler, Boston

THE Registration Desk will be located on the Mezzanine Floor, and all who attend the meeting are requested to register.

Owing to the lack of personnel and food supplies, the Hotel Statler must be informed concerning the number of members who will attend the various luncheons and dinners. Attendance is not limited, but tickets *must* be obtained in advance. It is doubtful whether any tickets will be available at the time of the meeting.

MONDAY EVENING, MAY 24

Annual Meeting of the Council of the Massachusetts Medical Society

- 5:00 **Supervising Censors' Meeting** (PARLOR D).
6:00 **Cotting Supper** (SALLE MODERNE).
7:00 **Council — Annual Meeting** (GEORGIAN ROOM).

TUESDAY MORNING, MAY 25

First General Session

GEORGIAN ROOM

Dr. Peirce H. Leavitt, *Chairman*
Dr. Leroy E. Parkins, *Co-chairman*

Symposium: Burns, with Special Reference to the Cocoanut Grove Disaster

- 9:00 *Burn Shock and Its Treatment.* Dr. Charles C. Lund: visiting surgeon, Boston City Hospital, and assistant professor of surgery, Harvard Medical School.
9:15 *Surface Treatment.* Dr. Oliver Cope: associate visiting surgeon, Massachusetts General Hospital, and assistant professor of surgery, Harvard Medical School.
9:30 *Chemotherapy.* Dr. Champ Lyons: assistant surgeon, Massachusetts General Hospital, and instructor in bacteriology and associate in surgery, Harvard Medical School.
9:45 *Respiratory Complications.* Dr. Maxwell Finland: chief, Fourth Medical Service, and associate physician, Thorndike Memorial Laboratory, Boston City Hospital, and assistant professor of medicine, Harvard Medical School.
10:00 *Pathology of Respiratory Burns.* Dr. Timothy Leary: medical examiner, Suffolk County, Southern Division.

- 10:15 *Medical-Examiner Service at the Disaster.* Dr. William J. Brickley: medical examiner, Suffolk County, Northern Division.

- 10:30 *Discussion.*

11:00 Annual Meeting of the Massachusetts Medical Society.

GEORGIAN ROOM

Annual Oration (following business meeting): *Small Puddles.* Dr. Edward P. Bagg, Holyoke: chief medical evacuation officer, Region II; president, staff of Holyoke Hospital.

Annual Luncheon (PARLORS A, B AND C): tickets **MUST** be procured in advance of the meeting.

TUESDAY AFTERNOON, MAY 25

Second General Session

GEORGIAN ROOM

Dr. Roger I. Lee, *Chairman*
Dr. Dwight O'Hara, *Co-chairman*

- 2:00 *The Medical Administration of Selective Service within a State.* Lt. Col. Victor D. Washburn, M.C., A.U.S.: state medical officer, Selective Service, Massachusetts.
2:20 *Current Considerations of the Army Anesthesiologist.* Major Stevens J. Martin, M.C., A.U.S., Fort Dix, New Jersey: chief of Section of Anesthesia and Section of Operating Pavilion Resuscitation and Oxygen Therapy, Tilton General Hospital.
2:40 *Cervical Spinal-Cord Injuries: A study of 101 cases.* Dr. Donald Munro: surgeon-in-chief and head of the Department of Neurological Surgery, Boston City Hospital.
3:00 *Wartime Responsibilities of the Public Health Service.* Dr. Warren F. Draper, Washington, D. C.: Acting Surgeon General, United States Public Health Service.
3:20 *Global Malaria.* Brig.-Gen. James S. Simmons, M.C., U.S.A., Washington, D. C.: director, Preventive Medicine Division, Office of the Surgeon General.
3:40 *The Increased Danger from Tropical Disease in the Present War.* Col. Richard P. Strong, M.C., A.U.S., Washington, D. C.: director, Division of Tropical Medicine, Army Medical School.

- 4 00 *How to Improve Fracture Results* Dr Charles L Scudder consulting surgeon, Massachusetts General Hospital
- 4 20 *Diverticulitis of Colon Its importance in general practice and its treatment* Dr Edward L Young surgeon in chief, Faulkner Hospital, and visiting surgeon, Massachusetts General Hospital, and Lieut Edward L Young 3d, MC, AUS, Boston
- 4 40 *Therapy of Hypertension* Dr Robert W Buck visiting physician, Pratt Diagnostic Hospital, and chief, Nephritic Clinic, Boston Dispensary

TUESDAY EVENING, MAY 25

7 00 Annual Dinner of the Massachusetts Medical Society

GEORGIAN ROOM

Tickets for the dinner MUST be procured in advance

Presiding Dr George Leonard Schadt, president, Massachusetts Medical Society

Guest speaker

Mr James A Hamilton, New Haven, Connecticut *president, American Hospital Association*, director, New Haven Hospital, and professor of hospital administration, Yale University

The Shattuck Lecture (SALLE MODERNE) (following annual dinner) *Physiological Considerations in the Treatment of Nephritis* Dr George W Thorn Hersey Professor of the Theory and Practice of Physic, Harvard Medical School, and physician in chief, Peter Bent Brigham Hospital

WEDNESDAY MORNING, MAY 26

Third General Session

GEORGIAN ROOM

Dr James W Manary, *Chairman*

Dr Edward J O'Brien, Jr, *Co-chairman*

- 9 00 *Newer Chemotherapeutic Agents* Dr Charles A Janeway assistant professor of pediatrics Harvard Medical School, visiting physician, Children's Hospital
- 9 20 *Modern Pharmacy and the Medical Profession* Mr Howard C Newton president, American Association of Colleges of Pharmacy, and dean, Massachusetts College of Pharmacy
- 9 40 *The Work of the Boards of Registration in Medicine and Nursing* Dr H Quimby Gallupe secretary, Massachusetts Board of Registration in Medicine, and secretary, Massachusetts Board of Registration in Nursing
- 10 00 *The Use of Refrigeration in Peripheral Vascular Disease* Dr F Everett O'Neil visiting sur-

geon, Boston City Hospital, and clinical professor of surgery, Boston University School of Medicine

- 10 20 *Newer Concepts of Gonorrhea* Dr Samuel N Vose associate professor of genitourinary surgery, Boston University School of Medicine
- 10 40 *Chronic Adhesive Subacromial Bursitis (Frozen Shoulder)* Dr Gilbert E Haggart attending orthopedic surgeon, New England Baptist and Deaconess hospitals, and chief of the Bone and Joint Service, Lahey Clinic
- 11 00 *Physical Therapy in Arthritis* Dr William B Snow, New York City associate in medicine, College of Physicians and Surgeons Columbia University, and director of physical therapy, Medical Center (Presbyterian and allied hospitals)
- 11 20 *Meeting Nutritional Requirements in Time of War* Dr Russell M Wilder, Washington D C chief, Civilian Food Requirements Branch United States Department of Agriculture
- 11 40 *Oxygen Therapy and Positive Pressure as Related to Gas Poisoning in War and in Civilian Disorders* Dr Alvan L Brach New York City associate professor of clinical medicine College of Physicians and Surgeons Columbia University

WEDNESDAY NOON, MAY 26

Section Meetings and Luncheons

12 00 m-2 00 pm

Tickets for the luncheons MUST be procured in advance

Section of Medicine

PARLORS B AND C

Dr Laurence D Chapin, Springfield *Chairman*

Major Richard P Stetson MC, AUS *Secretary*

The Problem of Civilian Medical Practice in Wartime
Dr John J Murphy Worcester

Section of Surgery

PARLOR A

Dr James C McCann Worcester, *Chairman*

Dr Oliver Cope Cambridge, *Secretary*

Surgical Lessons of the Pearl Harbor Attack Dr John J Moorhead, New York City professor of surgery, New York Postgraduate Medical School and Hospital, and director, Department of Traumatic Surgery (retired)

Section of Pediatrics

THE JUNIOR LEAGUE, 270 MARLBOROUGH STREET

Dr James M Baty, Belmont and Brookline, *Chairman*

Dr Gerald N Hoefel, Cambridge, *Secretary*

Nephritis in Childhood Dr Allan M Butler

Section of Obstetrics and Gynecology

WOMEN'S EDUCATIONAL AND INDUSTRIAL UNION
264 BOYLSTON STREET

Dr. Christopher J. Duncan, Waban, *Chairman*
Dr. Arthur F. G. Edgelow, Springfield, *Vice-chairman*
Dr. George Van S. Smith, Brookline, *Secretary*

Round-Table Discussion: Recent improvements in obstetric technic. Dr. Raymond S. Titus, Boston; Dr. Joseph W. O'Connor, Worcester; and Dr. Arthur F. G. Edgelow, Springfield.

Section of Radiology

HOTEL STATLER

Dr. Joseph H. Marks, Newton, *Chairman*
Dr. Stanley A. Wilson, Marblehead, *Secretary*

Pancreatic Achylia. Dr. Edward B. D. Neuhauser and Dr. Sidney Farber.

Section of Physiotherapy

PARLORS D AND E, HOTEL STATLER

Dr. Henry A. Tadgell, Winchester, *Chairman*
Dr. Wilmot L. Marden, Lynn, *Secretary*

Motion-Picture Program Relating to Physiotherapy.

Section of Dermatology and Syphilology

HANCOCK ROOM, HOTEL STATLER

Dr. J. Harper Blaisdell, Boston, *Chairman*
Dr. G. Marshall Crawford, Lincoln, *Secretary*

The Local Use of Sulfonamide in Dermatoses. Dr. Harold N. Cole, Cleveland: professor of dermatology and syphilology, Medical Department, Western Reserve University.

WEDNESDAY AFTERNOON, MAY 26

Fourth General Session

GEORGIAN ROOM

Dr. Charles E. Mongan, *Chairman*
Dr. Frank R. Ober, *Co-chairman*

2:00 *Prevention of Vitamin Deficiencies in Wartime.* Dr. Franz R. Stenzel: visiting physician, Newton Hospital.

2:20 *Present-Day Rapid Methods of Treating Syphilis.* Dr. Harold N. Cole, Cleveland: professor of dermatology and syphilology, Medical Department, Western Reserve University.

2:40 *Practical Importance of the Rh Factor in Obstetrics.* Dr. Paul Gustafson: assistant in obstetrics, Harvard Medical School.

3:00 *Cancer of the Larynx.* Dr. LeRoy A. Schall: professor of laryngology and professor of otology, Harvard Medical School, and chief of otolaryngology, Massachusetts Eye and Ear Infirmary.

3:20 *Epidemic Keratoconjunctivitis.* Major Murray Sanders, M.C., A.U.S., New York City: member, Neurotropic Virus Commission, Board for the Investigation of Influenza and Other Infectious Diseases in the Army.

3:40 *Endocrine and Pseudoendocrine Problems in Childhood.* Dr. Richard Wagner: assistant professor of pediatrics, Tufts College Medical School, and physician, Boston Floating Hospital.

4:00 *The Shock Treatment in the Psychoses.* Dr. Abraham Myerson: professor (emeritus) of neurology, Tufts College Medical School; clinical professor of psychiatry, Harvard Medical School, and director of research, Boston State Hospital.

4:20 *The Medical Profession's Responsibility in the Prevention of Blindness.* Dr. Hugo B. C. Riemer: consultant ophthalmologist, Massachusetts Eye and Ear Infirmary, and supervising ophthalmologist, Massachusetts Division of the Blind.

4:40 *Blood Pressure Determinations by Patients with Essential Hypertension: Evaluation of sympathectomy over a three-year to five-year period.* Dr. David Ayman: instructor in medicine, Tufts College Medical School, and associate physician, Beth Israel Hospital; and Dr. Archie D. Goldshine: assistant physician, Beth Israel Hospital.

Scientific Exhibits

BALLROOM ASSEMBLY

- | | |
|-----------------|---|
| Booth
S-9-10 | <i>Anesthesia.</i> Massachusetts members of the New England Society of Anesthesiology. |
| S-11 | <i>Technical Errors in Chest Roentgenography.</i> Massachusetts Tuberculosis League. |
| S-12 | <i>Serving and Conserving the Nation's Health.</i> Massachusetts Hospital Service, Incorporated (Blue Cross). |
| S-13 | <i>Your Plan for Surgical Care.</i> Massachusetts Medical Service (Blue Shield). |
| S-14-15 | <i>First Aid in Fractures.</i> Massachusetts Committee on Fractures and Trauma, American College of Surgeons and Boston Metropolitan Chapter, American Red Cross. Demonstration of first aid by members of the American Red Cross Motor Corps (Boston and Newton chapters). |
| S-16 | <i>Industrial Dermatitis.</i> American Medical Association. |
| S-17 | <i>Use and Abuse of Barbiturates.</i> American Medical Association. |

- S-18 *Blood for Victory* Blood Donor Center, Boston, Metropolitan Chapter, American Red Cross
- S-19 *Modern Pharmacy* Massachusetts State Pharmaceutical Association
- S-20 *Surgery of the Forearm and Hand* Second Surgical Service, Carney Hospital Exhibitors Dr William E Browne Dr John J Todd and associates

S-21-22-23 *Health in Child Care Centers* Massachusetts Department of Public Health

S-24 *Lesions of the Lung and Mediastinum* Lihey Clinic Exhibitor Dr Ralph H Adams

S-25-26 *Carcinoma of the Colon and Rectum* Lahey Clinic Exhibitors Dr Frank H Lahey and Dr Richard B Cattell

S-27 *Chemistry of Vitamin K and Synthetic Hormones* American Medical Association

S-28 *Prevention of Blindness* Department of Education, Commonwealth of Massachusetts Exhibitor Division of the Blind

S-33 *Veneral Disease Control* Health Department, City of Boston Exhibitors Dr G Lynde Gately, commissioner Dr John T Foley, director

Motion Picture Program

LOWER LOBBY

Tuesday, May 25

- 9 30-10 00 *Single Stage Lobectomy for Bronchiectasis*
- 10 00-10 30 *Occupational Dermatitis*
- 10 30-11 15 *Peptic Ulcer*
- 11 15-11 45 *Spinal Cord and Cauda Equina Injury*
- 11 45-12 00 *Compound Depressed Fracture of the Skull*
- 2 00-2 45 *Modern Diagnosis and Treatment of Syphilis*
- 2 45-3 30 *Anemia*
- 3 30-4 00 *Cholelithiasis with Common Duct Stone*
- 4 00-4 15 *Thrombi and Emboli*
- 4 15-4 45 *The Story of Lyotac—Normal Human Plasma*

Wednesday, May 26

- 9 30-10 00 *Mechanism of the Heart Beat and Electrocardiography*
- 10 00-10 15 *Post Partum Hemorrhage*
- 10 15-10 30 *Subtotal Thyroidectomy for Hyperthyroidism*
- 10 30-10 45 *Subtotal Hemithyroidectomy*
- 10 45-11 00 *Lumbar Sympathetic Ganglionectomy*
- 11 00-11 15 *Purposeful Splinting Following Injuries of the Hand*
- 11 15-11 45 *Treatment of a Normal Breech Presentation*
- 2 00-2 15 *Indirect Inguinal Hernia Anatomical aspects*

- 2 15-2 30 *Indirect Inguinal Hernia Clinical aspects*
- 2 30-2 45 *Indirect Inguinal Hernia Operative technique*
- 2 45-3 00 *Complete Laceration of the Perineum*
- 3 00-3 30 *Treatment of Asphyxia Neonatorum*
- 3 30-4 00 *Treatment of Burns of the Hand*
- 4 00-4 30 *Surgical Treatment of Varicose Veins and Ulcers*

Technical Exhibits

BALLROOM

	Booth No
Alkalol Company	14
American Hospital Supply Corporation	40
Ayerst McKenna & Harrison	26
The Baker Laboratories	39
Rudolph Beaver Inc	53
Billhuber-Knoll Corporation	41
Ernst Bischoff Company, Inc	24
The Borden Company	20
Brewer and Company	9 and 10
Buffingtons, Inc	46
Burroughs Wellcome & Co (USA), Inc	31
Camel Cigarettes	15 and 16
Carnation Company	11
Certified Milk Producers Association	S-1
Children's Incorporated	18
Ciba Pharmaceutical Products, Inc	48
Coca Cola Co	S 7 and 8
Crosbie-Macdonald	13
Davies, Rose & Company, Ltd	47
Doho Chemical Corporation	56
Effervescent Products, Inc	S 31
J H Emerson Co	S 37
C B Fleet Company	51
Gerber Products Company	29
J E Hanger, Incorporated	61
H J Heinz Company	S 5
Hoffmann-LaRoche, Inc	12
Horlick's Malted Milk Company	22
Hudnut Institute for Dermatological Research	7 and 8
Jones Metabolism Equipment Company	23
The Junket Folks	36
Kellogg Company	49
Lederle Laboratories, Inc	45
Eli Lilly and Company	50
M & R Dietetic Laboratories, Inc	25
F F Mahady & Company	37-38
Mead Johnson & Company	58-59
Medical and Surgical Relief Committee of America	6
Medical Protective Company	30
Mellin's Food Company	35
E. L. Patch & Company	S 2
Pet Milk Sales Corporation	28
Petrogalar Laboratories	32
Philip Morris & Co., Ltd., Inc	52
Picker & Ray Corporation	14
S M A Corporation	34
Sandoz Chemical Works Inc	44
G D Searle & Company	43
Sharp & Dohme, Inc	55
Smith, Kline and French Laboratories	S 4
Spencer, Inc	S 3
F R Squibb and Sons	33

The Sun-Rayed Company	17
Surgeons' and Physicians' Supply Company.....	60
Tailby-Nason Company	27
White Laboratories	42
Winthrop Chemical Company, Inc.	54
John Wyeth & Brother, Inc.	57

HARVARD MEDICAL ALUMNI ASSOCIATION

The annual meeting and dinner of the Harvard Medical Alumni Association will be held at 7:00 p.m. Wednesday, May 26, at the Harvard Club of Boston. Reservations *must* be made in advance through the executive secretary, Mrs. K. B. Wilson, Harvard Medical School (LONGwood 2380).

MASSACHUSETTS MEDICO-LEGAL SOCIETY

A meeting of the Massachusetts Medico-Legal Society will be held on the fourth floor of the Hotel Statler at 2:00 p.m., Tuesday, May 25 (the room number can be obtained at the Information Desk, Hotel Statler).

NEW ENGLAND SOCIETY OF ANESTHESIOLOGY

The New England Society of Anesthesiology will hold a luncheon meeting on the fourth floor of the Hotel Statler, from 12 noon to 2:00 p. m., on Wednesday, May 26 (the room number can be obtained at the Information Desk, Hotel Statler). The guest speaker will be Major Stevens J. Martin, M.C., A.U.S., of Fort Dix, New Jersey.

WAR ACTIVITIES

CIVILIAN DEFENSE

PENNANT TO IDENTIFY VEHICLES IN BLACKOUT

A uniform system of identification of emergency vehicles to enable them to operate during real or practice air-raid alarms was announced by the Office of Civilian Defense, Washington, D. C., in Operations Letter No. 111.

The primary identifying device is a white pennant measuring 18 inches along each side with a 6-inch basic Civilian Defense insignie, that is, the letters "CD" in red inside a white triangle superimposed on a red circle. The pennant is to be attached to the left front portion of the vehicle.

To identify emergency motor vehicles at night, the operations letter further prescribes a mask to be used over the right headlight. This mask may be made of any opaque material that can be easily, quickly and securely fastened to the headlamp. It is intended for use where blackout regulations permit the use of headlights; in coastal dimout areas it should be used in conjunction with dimout equipment. The design of the mask embodies the "CD" insignie 2½ to 3 inches in diameter in green.

Vehicles entitled to use the emergency identification include the following: vehicles of the armed forces of the United States or of her allies or other vehicles acting under orders or traveling with permission thereof; vehicles of fire departments and governmental police agen-

cies; ambulances and rescue cars and other vehicles converted to such use in emergency services; public-utility repair vehicles operating in emergency service; and vehicles in emergency service as defined by state Civilian Defense authorities.

Use of the pennants and masks described was made mandatory for the 16 states and the District of Columbia in the Eastern Defense Command in an administrative order issued by the director of Civilian Defense in accordance with the new air-raid protection regulations that went into effect on February 17. The letter recommends that all states adopt the definition of emergency motor vehicles and the methods of identification prescribed. Although many states have already adopted different methods of identifying emergency motor vehicles, it was urged that all states adopt the new devices. It was pointed out that a uniform system is particularly important in order that emergency motor vehicles that may be crossing state lines may not face unnecessary interference.

MISCELLANY

DR. ROBERTS DECORATED

Lieutenant Charles P. Roberts (MC), U.S.N.R., a Boston physician and an instructor (on leave of absence) at Tufts College Medical School, has recently been awarded the Silver Star Medal for gallantry and intrepidity in action during naval landing operations in French Morocco last November. The citation reads, in part, as follows: "The courage, leadership and professional skill of Lieutenant Roberts were outstanding and in keeping with the highest traditions of the naval service."

NOTE

Dr. William E. Ladd, William E. Ladd Professor of Child Surgery, Harvard Medical School, and head of the Surgical Service, Children's Hospital, recently gave the first Béla Schick Lecture at Mount Sinai Hospital, New York City, the subject being "Time and Choice of Operation in Early Life." This lectureship, founded in honor of Dr. Schick, formerly physician-in-chief of the Mount Sinai Hospital, has been made possible by a fund established in 1942 by his friends and associates.

CORRESPONDENCE

TUMOR DIAGNOSIS SERVICE

To the Editor: The State Tumor Diagnosis Service, which has been located since its foundation in the Huntington Hospital of the Harvard Cancer Commission, will move on May 10 to Room 387, Building E-2, Harvard Medical School. The telephone number will remain the same (LONGwood 4343). Specimen containers may be obtained from the Department of Public Health, 527 State House, as in the past.

The Tumor Diagnosis Service will continue to function as a center to aid the physicians and hospitals in Massachusetts in the pathologic diagnosis of tumors or of material suspected of origin from tumors. This service is rendered without cost. The expense is defrayed by the Department of Public Health of the Commonwealth of Massachusetts and by the Harvard Cancer Commission. Under ordinary conditions specimens will be processed and the report mailed out within twenty-four hours after being received.

SHIELDS WARREN, M.D.

695 Huntington Avenue
Boston

REPORT OF MEETING

SUFFOLK DISTRICT MEDICAL SOCIETY

A regular meeting of the Suffolk District Medical Society was held at the Boston Medical Library on October 28, 1942, with Dr James P O'Hare presiding. The program was a symposium on war gases.

The first speaker, Dr Granville A Bennett, had as his subject "Pathologic Changes Induced by Chemical Agents of Warfare." The various agents can be grouped, on the basis of their principal physiologic effects, into three main categories: vesicants, including mustard, lewisite and ethyl dichlorarsine, lung irritants, exemplified by phosgene and chlorine, and harassing agents, including the lacrimators, sternutators and screening smokes.

All lung irritants are to be regarded as acid gases. They primarily affect the respiratory tract. Chlorine produces its most pronounced effect on the mucous membrane of the upper respiratory passages, whereas phosgene injures the small bronchioles, alveolar ducts and alveoli. The principal pathologic changes are mucosal congestion with or without hemorrhage, pulmonary edema, atelectasis and emphysema. Physiologically, there are decreased aeration and impaired circulation. The injured lungs are susceptible to secondary infections, notably bronchitis and bronchopneumonia.

The vesicants injure any tissues with which they come in contact either in liquid or in vapor form. Mustard gas causes little or no immediate irritation. It produces skin burns that lead to progressive vesicle formation over a period of twelve to thirty six hours; these vesicles usually reach their maximal size in forty-eight hours. The vesicular fluid is clear and contains no trace of the agent. The burn causes much less discomfort than a thermal burn of similar extent. The lesion does not extend below the subcutaneous fat. Healing is slow. Lewisite acts much more rapidly than mustard gas and causes more marked symptoms of pain and tingling. Furthermore, the lesions penetrate to a great depth. If applied to the skin of the abdomen of a rabbit, the agent produces burns that extend into the peritoneal cavity and affect the liver or intestines. The vesicants produce pronounced necrotizing lesions in the upper respiratory tract. Secondary infections in the lungs, especially multiple lung abscesses, are prone to develop.

The treatment of persons contaminated with vesicants must be carried out immediately. Unless the agent is removed or neutralized within five minutes, a burn will develop. After fifteen to thirty minutes, prophylaxis is ineffective. The liquid agent should be quickly sponged off with any absorbent material at hand. Care should be exercised to prevent spreading the agent. A neutralizing agent should then be applied. Any commercial laundry bleach (sodium hypochlorite) may be used for mustard gas. Hydrogen peroxide, preferably 8 per cent strength, should be used for lewisite. These agents should not be used in the eyes, which should be washed quickly with running water or irrigated with a 1.5 to 2.0 per cent solution of bicarbonate of soda.

Dr Bennett described the construction and operation of cleansing stations such as may be needed at hospitals to receive injured and contaminated casualties.

Dr Andrew Contratto discussed the topic "Diagnosis and Early Treatment of Pulmonary Gas Casualties." The primary effect of gases is on the pulmonary system, the cardiovascular manifestations being secondary. Phosgene is the most likely gas to be used. Its odor, which is the

best means of identification, is like that of musty hay. Early, there may be slight eye irritation, cough and nasopharyngeal irritation. In heavy doses there may be nausea and vomiting. Often the victim may be aware of nothing, unfortunately. There is a latent period of four to forty-eight hours. Cough is usually present after about nine hours and is soon followed by cyanosis. The appearance is that of cardiac failure, with frothy sputum, pulmonary edema and rales, and asthma. The treatment consists of immediate and absolute rest in bed as soon as it has been established that a person has been exposed. Physiologically, there is early hemoconcentration. The degree of this phenomenon is a good prognostic index. The plasma protein is unchanged or diluted, which probably indicates extravasation into the areas of the pulmonary edema. The latter finding accounts for most of the manifestations. The stage of blue cyanosis is the equivalent of hemoconcentration. Therefore, treatment should consist of inhalations of 100 per cent oxygen, venesection of 500 cc (several times a day, if necessary), bedrest, heaters, the Trendelenburg position, the use of digitalis if the patient is old or known to have cardiac disease, and the use of aminophyllin if he is known to be asthmatic. The use of morphine is still a moot point, but the drug can probably be employed in small doses. The onset of gray cyanosis, which may even be primary if the hemoconcentration is sufficiently high, is akin to clinical shock and is invariably a premonitory sign of impending death. Treatment is similar to that for shock. In phosgene poisoning 80 per cent of the deaths occur in the first twenty-four to thirty-six hours, whereas in mustard gas poisoning only 3 per cent of the deaths occur in a similar period.

Dr Maxwell Finland next discussed the subject "Secondary Pulmonary Infections." Previous reports show that 22 per cent of the deaths from mustard gas occur on the fifth day, whereas 60 per cent occur in the next five days. Infection plays a definite role in at least 75 per cent of these cases. Heart failure is often a factor and may be precipitated by pulmonary fibrosis. Mustard gas frequently leads to chronic bronchitis and emphysema, with disability for eight to ten years. The question whether tuberculosis may be a result is still unsettled, but there is some evidence that arrest or quiescent cases may be reactivated. Delayed pulmonary irritation is especially likely to lead to secondary infection. Acute and persistent pulmonary disease is particularly prevalent in those who have been gassed. Fibrosis appears to be a great factor. The changes seen in such lungs are similar to those found following the pandemic of influenza. The most commonly encountered bacteria are the hemolytic and indifferent strains of streptococcus, and the higher types of pneumococcus, which comprise the usual mouth flora. Staphylococcus is relatively rare, but when present leads to the serious sequelae of necrosis, abscess and bronchiectasis. Much depends on the past history of the patient regarding exposures. The secondary invaders may follow an epidemic, such as one of measles, streptococcus throat or pneumonia. The treatment is the same as for any secondary infection. Early recognition depends on an elevation of the temperature, of the white-cell count and of respirations and on increased malaise. Chemotherapy should be given early, since the mortality may be lowered by diminishing the number of secondary infections. This type of treatment may also decrease the number of chronic cases, the complications and the spread. The drugs of choice in staphylococcal infections are sulfadiazine

and best food for insane persons" and, second, that it was "in the neighborhood of 'Genteel Society.'"² The actual reason for selecting Portsmouth as given by the opponents of locating the asylum there was that the superintendent of the Vermont Asylum for the Insane in Brattleboro, near the New Hampshire line, who was also on the committee, favored the Portsmouth location because it placed the hospital at the eastern end of the state and thus did not infringe on the territory covered by the other hospitals.³

Before the asylum building was completed, Dr. George Chandler was selected as superintendent because of his several years' experience at the Worcester Asylum in Massachusetts. Dr. Chandler's first report throws considerable light on psychiatric standards of that era. All New England institutions were still young—McLean at Charlestown, the oldest, was twenty-four years old, the Hartford Retreat was eighteen years old, just about reaching maturity, the Worcester Asylum ten, the Vermont Asylum six, and the Maine State Asylum, the youngest of the group only two years old—a mere nursling. The heads of these hospitals had little previous training in the treatment of insane patients, but they made up for this shortcoming by their enthusiasm and love for their work and by their realization that they had a job to do in a virgin field. The entire group objected to the therapeutic standbys of that era of puking, purging and bleeding. Nonrestraint was the byword, and in some cases was carried to extreme in allowing disturbed patients to harm themselves and others. There was free exchange of information regarding new methods of treatment of insanity among the superintendents of New England asylums, and a summary of changes in the methods of treatment and report of advances was annually recorded in the superintendent's report to the trustees of the asylum. The newly published *American Journal of Insanity*, whose beginning dates back to 1844 and which is the oldest specialty magazine in the United States, has played an important part in helping to promote interest in this specialty and to disseminate new information among asylum staffs all over the country. Many of the data of this paper have been drawn from the above sources.

Dr. Chandler reported on July 1, 1843, that the total admissions to the asylum were 76 during the first seven months of its existence. At the end of this time 22 inmates were discharged as recovered and improved and 6 as not improved; 1 died, and 47 remained in the asylum.

The price charged was \$2.50 a week for out-of-state patients, and \$2.25 for patients living in the state. For this, according to the report of the

board of trustees, they were furnished with board, washing, mending of their clothes, fuel and light, medicine, the services of experienced and faithful nurses and attendants, the constant attention and watchfulness of the physician, means of riding and other exercise and amusement.⁴

In a discussion of the causes of the attacks, Dr. Chandler reported that the most prominent cause, as given by the patients' friends, was religious excitement. He records 21 patients as rendered insane by this cause. Ill-health brought 14 per cent of the patients to the hospital in the seven-month period; intemperance was the cause of admission in 4 per cent, slightly less than the present figure of 6 per cent, and injuries to the head, fever, fits and pecuniary embarrassment and domestic affliction in 4 per cent each. In 25 per cent of admissions the cause was unknown. The large number of admissions as a result of religious excitement was a rather unusual occurrence, even in a period when religion occupied a much greater part of people's waking existence than it does now, and the cause of this epidemic of mental illness was the wave of Millerism or the Miller delusion that was sweeping the eastern states at that time.

* * *

The year 1842 saw the rise of Millerism, or Second Adventism, to its peak. It fell gradually after William Miller's prophecy that the end of the world would come in April, 1843, did not materialize. Religion in New England was a serious matter in 1842. The Devil, life hereafter, retribution for one's sins, were not preoccupations for Sundays only. Therefore when William Miller announced his end-of-the-world prophecies, he attracted wide attention all over New England, and through his lectures in Hampstead, Portsmouth, Exeter, Franklin and Concord developed many followers.⁵ A number of them were unable to stand the stress and strain of the expectation of the oncoming holocaust, and many broke down mentally. Fortunately, the newly opened asylum was ready to receive those most seriously affected. In most of the 21 patients admitted for religious reasons, the admission diagnosis was Millerism. In 1847, four years after Miller's prophecy failed to materialize, this percentage dropped to 5 per cent. The first patient admitted came for reasons of Millerism, and one can imagine Dr. Chandler's consternation when the Millerites, as they were then called, had to be admitted to the hospital in rapid succession, so that nearly one out of every three patients was a victim of this epidemic of mental disease. Dr. McFarland, the successor of Dr. Chandler in the superintendency, summarized as follows, in his 1852 annual report, the situation faced by Dr. Chandler:

Current popular delusions usually leave the most enduring traces on the records of lunatic hospitals. The first page of entries of the Folio Records of the Asylum commencing with the 29th of October, 1842, and terminating February 25, 1843, is a page of instructive history that has no precedent or analogy. History records many instances of the insanity that has suddenly affected multitudes, but all failed to leave so sad a history written as this volume will preserve of the Miller Delusion which was just reaching its acme as the doors of this institution were thrown open to receive its infatuated victims.

In a previous report, I⁶ have pointed out the manic depressive character of most of the patients admitted to the asylum because of the Miller delusion. Nearly all these patients made a good recovery after they were taken away from their environment and the surrounding religious excitement. A number of them, however, as is common with manic depressives, were returned to the hospital at a later date, oftentimes expressing the same religious delusions as on previous admission, although the second admissions took place in some cases from ten to twenty years after the first attack. That the Miller delusion phenomenon was not confined to New Hampshire is evidenced by the following editorial that appeared in the *American Journal of Insanity* in January, 1845:

If Millerism is understood the religious doctrine of the immediate destruction of the world—which has been extensively taught in this country by Mr. Miller and others, for two or three years past

We do not intend to give a history of it or to show that it is but the revival of a delusion which has often prevailed before to the great injury of the community. The evil results from its recent promulgation are known to all, for we have scarcely seen a newspaper for some months past but contains accounts of suicide and insanity produced by it.

Before us is a paper from the interior of this state published in November, which says: Our exchange papers are filled with most appalling accounts of the Miller Delusion. We hear of suicide, insanity and every species of folly. Another, a Boston paper makes a similar remark and says: One lady, one gentleman belonging to this city, were committed to the insane hospital last week from the influence of this horrible delusion. The man cut his throat but was stopped before he severed the large blood vessel. Another man cut his throat from the same cause causing instant death.

Like accounts we find in the Connecticut Philadelp^hia Baltimore and other papers. To this we might add that we have seen a considerable number of individuals who became deranged upon attending the preachings of this doctrine, most of whom have recovered though we have some now under our care whom we consider incurable, and have admitted two deplorable cases within a few days.

By looking at the reports of the lunatic hospitals in the northern states we notice that into three of them 32 patients were received during the last year while in unity was attributed to Millerism.

Allowing something for the exaggeration and mistakes in the accounts of the evils that have resulted from the inculcation of this doctrine, it must be evident to all that they are alarming. But in our opinion the country has as yet seen only a small part of the evils this doctrine has produced. Thousands who have not yet become deranged, have had their health impaired to such a degree as to unfit them for the duties of life forever, and especially is this the case with females. The nervous system of many of those who have been kept in a state of excitement and alarm for months has received a shock that will pre-dispose them to all the various and distressing forms of nervous disease and to insanity, and will also render their offsprings born hereafter, liable to the same.

We have no hesitation in saying that in our opinion the prevalence of the yellow fever or of the cholera has never proved so great a calamity to this country as will the doctrine alluded to.

Fortunately the dire predictions of Dr. Amariah Brigham, the writer of this editorial, failed to materialize. Millerism was soon forgotten, and in 1852 Dr. McFarland noted:

It will be observed—perhaps with a smile—that Spiritual Rappings as the current instance in point has furnished us its small quota of patients.

The victims of the *isms* of the day are either of the class in whom but a breath is necessary to submerge frail reason, or else of grade with him

who never had a dozen thoughts

In all his life and

never changed their course

Therapy consisted mainly in taking the patient away from his environment, attending to his physical needs, occupying him with useful tasks to prevent excessive self absorption and applying psychotherapy, then described as 'moral persuasion'. The results were quite satisfactory considering the asylum's resources, and although the figures for recoveries in a number of asylums exceeded those that were ever obtained in any mental hospital since, and were occasionally padded so that visits home or brief paroles were counted as recoveries, thus making it appear that recoveries frequently equaled admissions in a single calendar year, this actually was not done with any evil intent. It was in a way a healthy sign, as some asylum superintendents hoped thereby to convince the public that insanity was a curable disease and that not everybody entering the asylum was entering a land from which no one returned alive. Such padding of statistics turned almost into a cult, and manipulation of figures by hospital superintendents became a commonplace occurrence in an attempt to impress their boards of trustees with the excellent results the hospital was achieving. This practice was criticized by a number of institutional heads including Dr. McFarland and later with statis-

tical data, was effectively debunked by Dr. Pliny Earle.⁸

That patients in those early days received excellent physical care is evidenced from the following extracts from Dr. McFarland's report in 1850.

Only two individuals were ever placed under restraint, and then only for the protection of others. A leather belt around the waist, with wristbands which loosely confine the hands, is sufficient for the purpose. For those inclined to tear their clothing, a mitten confined to their hand is put on.

Our diet is always abundant, and of the best quality. The best of meats and the choicest brands of flour only are used. But one kitchen supplies the whole establishment, the officers, attendants and patients partake of the same food.

From the many who formerly enjoyed the Asylum's benefits, we often receive visits, letters and tokens of kindly remembrances, which evince the strong hold the institution has upon their grateful esteem.

Dr. McFarland resigned from the superintendency in 1852, afterward to become superintendent of the Illinois Asylum for the Insane. He was succeeded by Dr. John F. Tyler, who headed the asylum until 1857. Dr. Tyler introduced a number of improvements in the hospital, installed fixtures for heating it with steam, and was instrumental in adding two wings to the hospital, so that at the time of his resignation the capacity had risen to 225 patients. Dr. Jesse P. Bancroft was selected by the board of trustees to assume the position vacated by Dr. Tyler when the latter left to take over the duties of superintendent of the McLean Asylum.

* * *

For a period of twenty-five years Dr. Bancroft guided the policies of the asylum, to be succeeded in 1882 by his son, Dr. Charles B. Bancroft, who continued as superintendent until his retirement in 1917. Thus the Bancrofts were connected with the hospital for a period of sixty years out of the one hundred years of its existence. With the exception of the Monro and Tuke families in Britain,⁹ and the Galt family in Virginia,¹⁰ this is one of the few instances where father and son were connected with a single mental hospital for such a long period of time. Dr. Jesse P. Bancroft was endowed with keen critical faculties, and he possessed excellent insight into the problems of his patients and the administrative difficulties that he encountered. He further enlarged the heating plant in the hospital, introduced artesian wells as a source of water supply for the growing institution, and fostered the idea of individual buildings for various types of patients instead of the single unit or Kirkbride type of building.¹¹ He was faced five years after he assumed office with the loss of some of his assistants as a result of the

Civil War, the threat of inflation, the rising cost of supplies and in fact all the problems that face hospital superintendents during the present war crisis.

In 1862, twenty years after the opening of the asylum, Dr. Bancroft reported that the resident population had risen to 196, or two and a half times the number admitted during the first year. Eighty-six patients were admitted during that year. Forty-one were discharged as recovered, 32 as improved, and 7 as unimproved, and 13 died. Dr. Bancroft noted:

A satisfactory success has followed the efforts for the restoration of our patients; and it is a matter of sincere pleasure that we are able to record an unusually large percent of recoveries, and among them are some so cheering that we may well regard our labors amply rewarded.

He deplored the lack of better facilities for occupational therapy but stated:

In pleasant weather much pleasure and benefit has been derived from exercise in the open air, in farming, gardening, walks and rides in the adjacent country, or those harmless games which are at once healthful and captivating. Much sewing, knitting, and similar work has been done by the female patients, which has a second value, great, though less than that accruing to the laborer herself. This is emphatically true of a considerable amount of sewing and knitting *done for the army*. *No occupation has seemed to afford them more unalloyed pleasure, than that done for the noble and self-sacrificing defenders of our country.*

The last remark indicates that the repercussion of the War between the States had also reached the walls of the asylum.

Dr. Bancroft's observation on the causes of insanity and the importance of early hospitalization were pregnant with ideas.

As with other diseases, a certain proportion of those attacked with insanity do not recover under any circumstances; nor does death come to remove them from the distracted life in which the disease has left them. These pass into the various chronic forms; in all of which reason, the guide of life, loses its control, and the subject passes under the control of the ever-changing impulses and the animal instincts. The tendency is ever toward a lower level—a state further removed from the normal standard of thought and action. Even in the wreck of reason and responsibility, Nature has kindly provided that the human being need not be wholly a wreck. Such is the organization, that, like an automatic machine, when the intelligent, directing mind is cast from its supremacy, still, under a law of habit, if the individual can be under the influence of another mind to keep him in motion, he will follow to a great extent the routine of ordinary life, when, without this exterior influence, he would subside into stupid inaction, and fall under the direction of the mere animal instincts. It is by availing themselves of this principle, that asylums,

in cases of the incurable, are able to transform what would otherwise be little more than existence into a life possessing many rational occupations and enjoyments. The constant presence of attendants and other guiding influences supplies this motive force

The other [cause] was acute pericarditis in a contraband from the State of Alabama, and directly from the fatigues and exposures of a forced march in Virginia. The disease was far advanced on admission, and terminated on the fifth day. The delirium for

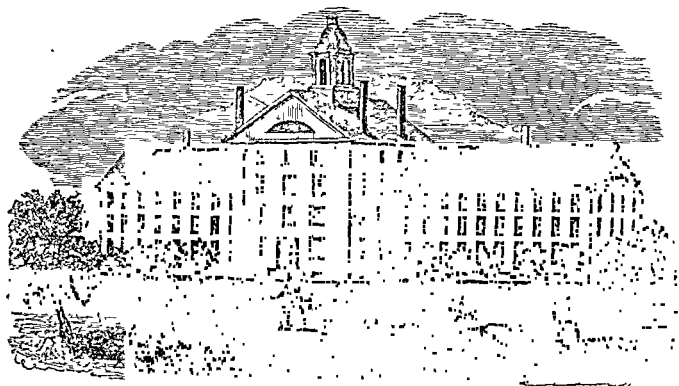


FIGURE 1. *New Hampshire Asylum for the Insane (1844)*

from without, this substitute for self-guidance, and thus there is kept alive a grade of habits and activities entirely impossible in the absence of these helps. This outside aid is to the demented what the splint is to the broken bone: without it the subject falls to the ground, but with it very respectable locomotion is secured.

In his report in 1864 Dr. Bancroft lamented the increase in cost of living as a result of the war, and the difficulty of making ends meet on a pre-war budget.

The very great advance in the price of labor, provisions and fuel, during the last eighteen months, has been sensibly felt at the Asylum, and has made it a difficult matter to support the institution from its current receipts. This statement will create surprise in the mind of no one. The fact is one incident to the war and to be often encountered elsewhere throughout the country. It may be more clearly appreciated however, by comparing the present prices of some of the leading articles of consumption, with the prices of the same articles one year ago. For this purpose your attention is respectfully invited to an examination of the following:

ARTICLES	PRICE JUNE, 1863	PRICE JUNE, 1864
Flour	\$7 50 per bbl	\$10 00 per bbl
Sugar	12½ cents per lb.	20 cents per lb
Tea	80 cents per lb	\$1.12½ per lb
Butter	18 cents per lb	30 cents per lb.
Cheese	10 cents per lb	18 cents per lb
Molasses	40 cents per gal.	80 cents per gal.
Wood	\$4 00 per cord	\$6 00 per cord
Labor	Twenty five per cent higher than one year ago	
Meat	Fifty per cent higher than one year ago	

The war also left its stamp on the hospital wards. In the causes of death for the year Dr. Bancroft reported:

which he was brought to us was a symptom of the acute disease and not insanity.

Psychiatry in 1860 consisted of a mixture of metaphysics, general medical precepts, a Hippocratic classification of most cases into mania or melancholia and many statistical data gathered in British, French and American asylums, but little of which could be applied successfully in the individual case. Here and there appears evidence of reluctance in accepting the immediate precipitating cause of an attack of mental illness as the most important etiologic factor, and some of the hospital records contain excellent descriptions of patients' symptoms and some new speculation as to the real cause. The therapeutic results were satisfactory with the means available at the time, but there was also an awareness in the minds of intelligent asylum physicians that with their present state of knowledge they could go so far and no farther.

In his report for 1866 Dr. Bancroft gave a lucid description of a case that was later classified by Kraepelin as dementia praecox and by Bleuler as schizophrenia, and also gave suggestions as to treatment that in the main have not changed in the last sixty years.

Still again there is the silent, undemonstrative individual, given up to a state of "brown study, distraction and reverie"—a waking dream which, if not broken in upon, works mischief to the brain and mind.

But, while the forms in which the diseases of the mind and feelings are manifested are almost without limit, one thing is true in all; namely, a morbid concentration of the thoughts upon self, with an intensity proportioned to opportunity. The mind inclines to retire within itself, shut out the rest of the world, unmindful of its true relations, and make self the center of all thought and interest.

The continuance of this state is fraught with danger to the integrity of the organism. The cerebral action by degrees becomes accommodated to it; the abnormal condition, becoming habitual, is continued into the chronic state, and is incapable of change.

It becomes, therefore, a leading object in treatment to interfere with this world of self—scatter its creations and fancies and people it with objects and thoughts foreign to its own.

Sleep therapy apparently is not new. In 1871 Dr. Bancroft wrote about a new and powerful drug, chloral hydrate, a boon to sleepless sufferers.

In this connection I will briefly refer to a medicinal agent recently added to our resources for the treatment of insanity, which has attracted so much attention as to give consequence to every careful observation of its use. Whether all that is claimed in its favor, on the one hand, or all the fears entertained in regard to its use, on the other, prove true, it is equally a matter of interest to the public, that the experience of those who have carefully used it should be placed on record. I refer to the Chloral Hydrate as a remedy for wakefulness.

We commenced the use of this drug a little more than a year ago. It being a powerful medicine, and new to physicians as such, we proceeded cautiously with the trial of it, selecting the cases with much care, and watching closely any effects produced. A special record was opened for the cases in which the chloral was used, and continued through the year. From our observations thus far, we have reason to be gratified with results.

Dr. Bancroft also appreciated the importance of habit pattern formation in mental illness, especially in recurrent cases such as those of manic-depressives, and the need of early treatment in such cases. Much of what he said anticipated Pavlov's ideas on conditioning as applied to psychiatric disorders. He discussed the problem at length in his 1879 report.

There are no inconsiderable number of persons in every community who suffer several fresh attacks of insanity during their lives. Still, those persons are essentially well between the insane intervals, and with others share the responsibilities and bear the burdens of life. Probably a large proportion of these each time lose something of their native mental vigor, though in some it is difficult to see it. It would seem that in many of these cases there is developed by degrees a tendency to the recurrence of the insane cerebral action; that this alternation gains the force of a habit, by the same law on which habits are formed in normal directions. In some, this ends in a pretty regular division of the remainder of life between the sane and insane states. If this tendency is once set up in the nervous system by the first occurrence of insanity,

the importance of a recognition of it cannot be overestimated. For, considering the physiological law of habit in the nervous system, intelligent effort at this period would be of much avail in warding off the evils which otherwise impend. Every act or influence tending to call into activity the morbid states should be studiously avoided; and everything favoring the continuance of healthy mental states should be as studiously cultivated and fostered. Some persons succeed in learning this lesson, and thus escape a second attack, but more do not; but, regardless of the relation of methods of living, as regards the appetites, the passions, and activities of life, to mental states, blindly overstep the bounds of prudence and are precipitated again into the insane state. At length, the recurrence is brought under the law of habit, and each time a less and less exciting influence is required, and the alternation comes to be almost automatic.

The importance of separating patients according to their mental condition and giving individual care to those who would benefit from it is emphasized by Dr. Bancroft in 1881.

More and more, each year, general routine methods are giving place to individual care and treatment—those more reliable have larger latitude, and self-dependence is trusted to the outer limit consistent with safety and a prudent regard to the liabilities in the case. It is easy to see how much more readily and effectively such a principle can be carried into practice with the help of properly adjusted buildings than in those so monotonous in construction as to enforce a disregard of the nicer differences in personal character and symptoms which any considerable number of cases is sure to present.

One of the indirect results of adopting this modified plan of buildings (as far as practicable) will be to diminish the contrast between life in the institution and ordinary domestic life. In the degree to which this can be done, will be lessened the reluctance felt to resorting to a public institution for care and treatment urgently needed, yet impracticable at home, both on the part of the patient and friends.

In his last annual report, written in 1882, Dr. Bancroft summarized the principles of therapy practiced by him during his twenty-five years of superintendency and compared it with standards used elsewhere. He was also free in his criticism, and was proud of the methods he had used in New Hampshire with so much success.

The same general plan of management adopted heretofore has guided our practice the past year. To state it in a word, we should say that the prime effort has been, leaving out all specific dogmas, routine methods and panaceas in management, to make each case an individual study, and then to adopt the course of treatment and care indicated by the facts in the case, so far as we have the means to do it. In this effort it is sought to signalize insanity as a thing by itself as little as possible; in all arrangements, to follow the ordinary usages of general society until compelled to make exceptions by the loss of self-controlling power on the part of the patient; and to trust the latter with all the responsibility he can safely bear. Thus, as much personal liberty is granted, and as little repression imposed, as possible, although it has

not been found practicable to discard all restraint. In settling questions of this class, the exercise of common sense on the actual facts in the case has been our reliance, in preference to any of the special dogmas which sometimes have gained a prominence out of

Thus Dr. Bancroft set forth a policy to which American psychiatry has wholeheartedly subscribed and which it has tried to follow. He also foresaw, however, the shortcomings of the methods of treat-

NEW HAMPSHIRE INSANE ASYLUM .		Page 1
No. 1	Name, <i>William Condit</i>	
Admitted <i>October 29</i>	1842	
Nativity,	Residence, <i>Wilmington</i>	
Name and Nativity of Parents,		
Civil Condition, <i>Married</i>	Occupation, <i>Farmer</i>	
Age, <i>25</i>	Height	Weight
Complexion		
Cause, Pre-existing, <i>Wilmington</i>		
<i>Disturbed mind disease</i>		
Existing <i>Wilmington</i>		
How admitted, <i>Friend</i>	No. of admission to this Asylum,	
Former case numbers with condition on discharge,		
Other hospitals,		
No. of attack	Duration, <i>Two weeks</i>	
Diagnosis on admission,		
Diagnosis on discharge,		
Discharged <i>January 5</i>	1843	Condition, <i>Improved</i>
Readmitted	18	No.

FIGURE 2. Admission Page from the Record of the First Patient to Be Admitted to the New Hampshire State Hospital

proportion to their real consequence. For example certain asylums in Scotland have become widely celebrated on account of the special prominence given to the circumstance of unlocked doors, even while that result is achieved by the device of a guard standing at each door to dispute the passage of any untrustworthy patient. While all practicable freedom is a thing most desirable, still, this show of it without the fact is to my mind a sadder shock to the sensibilities than the lock for which the guard is made a substitute. A deceptive offering of what is not really granted is the most objectionable of measures. This practice is more attractive in the abstract than in the concrete.

ing the insane *en masse*, a tendency that became strongly apparent in a number of states for the next fifty years as a result of poor facilities for patients, shortage of physicians and general indifference. The following paragraph expressed his final opinion in this matter.

A careful observation of the current history of the hospital life of the insane for the last twenty-five years has left upon my mind the firm conviction that the true germ—the animating principle of the improved management of the insane in hospitals at the present time, as also its promise for the future—is

the growing recognition of the individual in dealing with the insane, in place of the old method of regarding them, for study and treatment, as a class. The old traditional theory practically treated them as a distinct group of mankind, with identical attributes and wants. The logical outgrowth of this doctrine was to provide for all similar surroundings, and subject all to identical regimen. Thus arose the huge classifications, wholesale methods and sameness of remedial appliances. On this plan the tendency was to sink the individual in the class, and run into a monotonous round of measures. In contrast with this, the modern, and I think the coming, view is to bring the individual to the front, not only in the study of individual symptoms of disease, but in the recognition of personal differences, constitutional and acquired,—differences of character, taste, habits of life, and the like,—as the rational criterion of the measures required to make treatment really remedial. Approaching the subject from this direction, the demand for great diversity of agencies and influences, growing out of the personal differences just alluded to, becomes imperative. The more this view is indulged, the more it appears to the hospital physician that instead of a homogeneous group to house, to feed, and to treat as a unit, he has a society, made up of persons varying indefinitely in characteristics, and varying as greatly in their requirements for successful remedial treatment as do the members of general society in their personal characteristics. Experience has taught nothing more clearly, than that if these personal differences are ignored and sunk in a routine, treatment fails to do its work.

Dr. Bancroft's successor, Dr. Charles P. Bancroft, or "young Bancroft," as he was then called, maintained the advanced policies of his father after assuming office in 1882. His annual reports continue to represent an exposition of the problems that confronted the American psychiatrist of that period. There was an attempt at continuation of sedation therapy by the use of chloral hydrate, trional and dormiol. In 1896 several papers appeared praising the use of thyroid extract in insanity. One by Dr. Charles G. Hill,¹² on observation of the effect of thyroid feeding on the insane, was followed by a longer study by Mabon and Babcock¹³ giving glowing reports of results obtained in a large number of cases. Also a paper by B. W. Stone on "Thyroid in Insanity" was presented at the forty-fourth annual meeting of the American Medico-Psychological Association in 1898, presenting additional evidence of beneficial results of the administration of thyroid extract, in doses of 30 to 60 gr. daily until the patient developed an elevation of temperature. Unfortunately, the final results were not any more lasting than those reported by Hoskins and Sleeper¹⁴ in 1930. Dr. Bancroft wrote in his annual report in 1900, "Thyroid treatment has been faithfully tried with but indifferent results." A number of records in the hospital of that period testify to the veracity of his conclusions.

Dr. Charles P. Bancroft was the first hospital head to organize a training school for nurses in New Hampshire. The school at the asylum was opened in 1888, and has continued to admit students for training uninterruptedly since that time. It was the second mental hospital in New England to open such a school for psychiatric nurses,¹⁵ the first school having been opened at the McLean Hospital in 1882.

The New Hampshire Asylum for the Insane under Dr. Charles P. Bancroft was also one of the few institutions that substituted Kraepelin's classification of mental disease for the outmoded Hippocratic classification of mania and melancholia followed before 1900. Although Kraepelin did not begin to formulate his ideas definitely until 1896,¹⁶ records in the state hospital in 1900 already displayed the new diagnostic classification.

In the meantime, the resident population of the hospital continued to increase. In 1902, twenty years after Dr. Charles P. Bancroft assumed office, and sixty years from the date of its opening, the population was nearly 500. There was no proportionate increase in the number of physicians, and a plaintive note appears in the reports bemoaning the fact that more funds will be required if the hospital is to maintain its standards. As in common with all the states at that time, the cry for economy was first practiced in the appropriations for state institutions, and the state hospitals were the first to suffer.

Although there was much activity in some institutions during the first two decades of the twentieth century, state-hospital standards in psychiatry failed to keep pace with the progress made in other specialties in medicine. Freud's work in psychoanalysis was becoming known, but was of little practical use in the large mental hospitals. Malaria therapy in neurosyphilis was introduced in the United States in the middle nineteen-twenties, but was not accepted in most hospitals until 1930. Individual therapy was less developed than it had been in the previous century, since there were more admissions to the hospitals, more patients per physician, more dependence on group therapy, and therefore less knowledge of the patient's individual problems. In the majority of institutions too much attention was being paid to classification, and at the end this procedure became almost a fetish. Much more time was spent on it than on actual therapy, and most frequently the classification of certain groups depended on local criteria and the individual physician's whims. Dr. Charles P. Bancroft¹⁷ fully appreciated this fallacy, and in a penetrating analysis pointed out how institutional incidence of certain types of mental illness in Massachusetts varied to

such an extent that in two neighboring state hospitals twice as many manic-depressive or dementia-præcox patients were admitted in one as in the other, although the population in both districts at that time was homogeneous. This analysis exposed the lack of knowledge of the exact etiology of mental illness, dependence on a descriptive classification to cover up such ignorance and a willingness to substitute a new terminology for actual search for further data.

The Laconia State School for the Feeble-minded came into existence in 1900, largely through the effort of Dr. Bancroft. Dr. Charles S. Little was the first superintendent, and after he organized the school his administrative ability was recognized and he was offered a position at Letchworth Village, New York, where he continued his excellent work. He was succeeded in the superintendency in 1910 by Dr. Benjamin W. Baker, who has ably continued at this task and is still in charge of the school.

The history of psychiatry in New Hampshire would be incomplete without mentioning the efforts of Mrs. Charles P. Bancroft. She played a large part in developing the training school for nurses at the New Hampshire Asylum, and was the prime mover for the organization of the Laconia State School for the Feeble-minded. She was also appointed a member of the first board of trustees of the school, and her influence was much felt in getting the new institution properly started. Intelligent, able and forceful, she belongs to the group of New England women which has produced a Dorothea L. Dix, a Linda Richards and a Lucy Blackwell. No wonder that when the editor of the *Manchester Union* was informed that the newly appointed board of trustees to the school consisted of three prominent male citizens and Mrs. Bancroft he reported, "Now the Laconia State School has a new Board of Trustees which consists of three weak-minded men and one strong-minded woman." It is thanks to much of the efforts of this strong-minded woman that New Hampshire has a good school for the feeble-minded, a hospital for women and children in Concord, a children's-aid society and many other charitable organizations to the development of which she has devoted much of her time and energy.

* * *

In 1917 Dr. Charles P. Bancroft retired, to be succeeded by the present superintendent, Dr. Charles H. Dolloff. The hospital population rose to 1233 in 1917 as a result of the State's taking over the care of many of the chronic insane who were previously cared for at the county farms. Another war was on, and Dr. Dolloff had to face

the loss of much of his personnel and a number of staff physicians, but the work at the hospital went on and the patients continued to receive excellent care.

The last quarter of a century has seen much progress in the therapy of mental illness. This advance is also reflected in the annual hospital reports. In 1928 the use of malaria in the treatment of neurosyphilis was introduced, to be superseded in 1934 by artificial-fever therapy. In 1930 the combination of carbon dioxide and oxygen was tried for the treatment of catatonia, but this was given up after a short time because of its limited value. Hoskins and Sleeper's¹⁸ enthusiastic report on the administration of thyroid extract in schizophrenia brought on a revival of this form of therapy, with results no better than those reported by Dr. Charles P. Bancroft in 1900. Psychoanalysis reached its heyday for a time in the thirties, when there were two analysts on the staff, but came to be disregarded later on as a doubtful and rather expensive therapeutic procedure for a state mental hospital.

Mental-hygiene clinics were first started by Dr. Dolloff¹⁹ in 1930, in the form of a clinic in Manchester held once a week. This clinic has since developed into a network of clinics embracing all sections of the state, requiring the services of several physicians and social workers and helping hundreds of children annually.

A law permitting the sterilization of patients in mental hospitals and schools for feeble-minded was passed in New Hampshire in 1917, after an elaborate survey of hereditary factors in mental illness in the state, inaugurated by Dr. Charles P. Bancroft in 1910. The law was modified in 1929, thanks to the efforts of Dr. Charles H. Dolloff, so as to increase its usefulness. As a therapeutic measure the law has proved of greater importance than it has as a eugenic one.²⁰

Dr. Dolloff's latest biennial report, published in 1940, gives a bird's-eye view of the problems faced by the hospital superintendent nearly a hundred years after the foundation of the asylum. He wrote as follows:

In our psychotherapeutic work we have been somewhat hampered by the small size of our medical staff, which makes it impossible to devote the individual attention to patients which would be desirable, though such attention has been given whenever possible. To compensate for this, group therapy has been extensively used. Such therapy has been greatly simplified as a result of the stability, the long years of training and co-operative spirit of the employed personnel of the hospital. Additional physicians to administer individual psychotherapeutic treatment are urgently needed.

Among the specific treatments employed with success in psychiatric conditions have been the following:

The use of Dilantin, largely replacing older methods of treatment, including phenobarbital, has greatly simplified the problem of epilepsy.

Though the use of insulin in the treatment of functional ailments has been largely given up because of the rather complicated preparation necessary for its use, Metrazol has been used extensively. While in all probability very few patients have been permanently cured as a result of the use of Metrazol, it has proven a very effective adjuvant for use in conjunction with other methods of treatment.

The use of chemotherapy and pyretherapy in the treatment of neurosyphilis has been continued and the results have been very gratifying. In many cases so treated apparent cures have been effected, and in practically all cases varying degrees of improvement have been noted.

The hospital has recently co-operated with the venereal-disease clinics of the state in giving preventive fever treatments to a number of potential neurosyphilitic patients.

We have attempted to keep abreast of general medical progress, and have taken advantage of new methods as they have developed. Among such methods might be mentioned: chemotherapy in infectious diseases, such drugs as sulfanilamide, sulfapyridine and sulfathiazole being used extensively; vitamin therapy, including intraspinal use of vitamin B, in chronic neurologic conditions; endocrine therapy, including the very recently developed and as yet unpublicized oral use of diethylstilbestrol.

If Dr. Chandler could visit the asylum today, he would find that the original unit that he helped to build to accommodate 96 patients had grown nearly ten times in size. Besides, ten other units have been added, and the total population of the hospital has risen to almost twenty-five times its original capacity. Dr. Jesse P. Bancroft's dream of individual buildings to take care of the various types of patients according to their needs has also come true. The number of permanent employees is six times the number of patients reported by Dr. Chandler to have been admitted during the first seven months of the asylum's life. Nurses have become an integral part of the hospital's therapeutic scheme, and Dr. Charles P. Bancroft's nursing school has grown and expanded, so that at present the hospital has the largest number of nurses per patient of any state hospital in the country.²¹ The ratio of physicians to patients is not so high as the superintendent would have desired, but economic and other factors prevented such an expansion, although the ratio still ranks among the highest to be found anywhere.²¹

Dr. Chandler would also find fever used as an ally instead of opposed as an enemy in the treatment of mental disease; electricity, harnessed by Dr. Rush's contemporary and townsman Benjamin Franklin, used for curative purposes, to "shake" some patients out of their attacks, and occasionally as a "tranquilizer"; artificially in-

duced sleep used to advantage; and a large variety of unheard-of chemicals replacing poppy extract, the standby of his era.

He would encounter much to be surprised at—yes—but he would also have some remarks of his own to offer before returning to his city of Worcester.

"Yes," he would say, "you have grown, no doubt. Your annual number of admissions is six times the total number of patients we had room for when the hospital was built. One out of four of your patients comes to you, however, because your houses are smaller, your living standards have changed, and old grandma or grandpa, if feeble and forgetful, is no longer wanted at home. You are not curing any more of them than we did in my day with good food, clean bedclothes and an occasional glass of port wine. Yes, it is nice to give them such good care in the hospital and leave the family free for work in the factory or in the field, and to find time to entertain friends or go to the flicker shows.

"We did not have much syphilis in my time, and then it only rarely affected the brain; and when it did cause paralysis, we knew there was no cure and let them die. You are doing good work in this field with your fever and drugs, but many of these patients who would probably have been better off dead now have their lives prolonged, only to remain permanent boarders in your hospital for the rest of their days, and of little use to themselves or to others.

"And as to those silent, undemonstrative patients, those sunk in 'the state of brown study, distraction and reverie' so well described by my successor Dr. Jesse P. Bancroft, you really seem to do a lot for them with electric shock, Metrazol shock, insulin shock, various sleep potions, water cures and other fancy treatments. This sort of treatment tranquilizes many of them when they are disturbed, and probably cures some. Our teacher, Dr. Rush,^{22, 23} had his own gadgets for such purposes; if they did not work he bled his patients, purged them, or made them puke. It quieted most of them, and as to the number of final cures produced by insulin, Metrazol or electric shock, let us wait for another twenty years before making a final appraisal. It might require the services of another physician like my successor, Andrew McFarland, or another Pliny Earle⁸ to unscramble and analyze some of the excellent results you are reporting now with all these newfangled methods, so as to determine whether another 'cult of curability' is not being fostered among you. It is possible that your actual percentage of recoveries is not much greater than that we obtained by removing the patient

from his home and from doting or obnoxious relatives, feeding him up well and keeping him busy, with the additional use of moral persuasion

"You call the latter 'psychotherapy,' and some of you claim spectacular cures for a branch of it called 'psychoanalysis' It takes a lifetime to cure a patient by this method, and at times you engrift a new illness to cure the original disease, such as the malaria you use to cure syphilis, but the results are not so good. You believe that mental evacuation or catharsis is good for a person—yes, if not carried to excess so as to produce a case of mental dysentery and perpetual dependence on the moral straightener—he a form of inseparable chamberpot—for constant support. You also claim that the old timers did not appreciate the importance of sex in the production of mental illness until it was rediscovered by a man named Freud²³ We knew as much about it, but our customs did not make it easy for us to discuss it as openly as you do, and, besides, a patient given a frank diagnosis without an easily available cure is at times worse off than one left in ignorance about his condition. Did not that grand old man in Burton²⁴ devote one third of his *Anatomy of Melancholy* to the description of the symptoms and cure of love melancholy for those who are able to read and understand between the lines? And as to the many cures reported with psychoanalysis, this matter will also require further rechecking, for the secretiveness of these moral straighteners makes it hard for the stranger like myself to find out whether another cult has not grown up among you. After all, there was Elisha Perkins,²⁵ ²⁶ the clever Yankee from Connecticut who for a time with his tractors, it was said, was just as adept in curing such illness as you and I, and there was that transplanted Viennese, Mesmer²⁷ whose personal success has never been equaled and who has taught us all what could be done with suggestion properly used; and that farmer from Alstead, Thomson,²⁸ with his water cures and herbs; and also that very successful neighbor from the hills of Bow, Mary Baker

Eddy.²⁹ Time will only tell whether there is really much justification for all that is claimed for this new brand of moral persuasion. In the mean time, you have the resources, the urge to find out and the material to work with. You are on the right road, and God bless you!"

1426 Elm Street

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THE MEDICAL MANAGEMENT OF INTESTINAL OBSTRUCTION*

With Special Reference to the Use of the Miller-Abbott Tube

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THE title of this paper is not intended to imply that intestinal obstruction is a medical problem alone, but it is meant to suggest that this condition may not be an acute surgical emergency such as it has been considered until a relatively recent date.

Strangulation of the bowel is still, and probably always will be, an indication for prompt surgical intervention. Early intestinal obstruction from an obvious cause such as external hernia is also a surgical problem. However, we have at our disposal today a means of decompression and readjustment of the altered physiologic state brought about by intestinal obstruction without resorting to surgery that should be well understood and utilized.

The mortality for nonstrangulated cases when treated by immediate surgery was formerly 30 per cent or more. The recent mortality with the use of nonsurgical methods of decompression, alone or in conjunction with surgery, is 10 per cent or less.¹⁻³ This dramatic reduction speaks eloquently for medical therapy.

There has been a great deal of surmise about the mechanism of death in nonstrangulated cases of intestinal obstruction. There were formerly numerous unsuccessful attempts to isolate a "toxic substance." With the early work of Hartwell and Hoguet⁴ followed by that of many others, the chemical investigations appeared that demonstrated the disturbed fluid, salt and protein balance. Intravenous alimentation became a common practice, but still there was no marked fall in the mortality rate. It remained for Wangenstein⁵ and Fine et al.⁶ to show the importance of simple distention as the key point from which the subsidiary physiologic and chemical changes had their origin. Abbott and Johnston⁷ were next able to demonstrate that when the distention was controlled and nutrition maintained, the patient could continue in good condition almost indefinitely in spite of a complete obstruction of the bowel. It is the decompression of the distended bowel, irrespective of the cause of the distention, that brings about the greatest improvement. The realization of this factor is responsible for the great reduction of

mortality in the treatment of intestinal obstruction.

Criteria for the diagnosis of intestinal obstruction have been laid down in all the textbooks. Colicky abdominal pain, abdominal distention, persistent nausea and vomiting eventually leading to the vomiting of fecal material, and obstipation are the usual symptoms. The patients appear sick and dehydrated and are often in shock. Auscultation of the abdomen reveals early generalized increased peristalsis, with the later development of peristaltic rushes, giving the characteristic tinkle of gas and fluid in a distended bowel and finally a completely quiet abdomen. The vital signs are usually moderately elevated and a slight leukocytosis is present.

X-ray examination may be of considerable help in establishing the diagnosis at an early stage. The accumulation of gas within the obstructed bowel is visualized by a flat film of the abdomen. Gaseous small-bowel distention presents the typical ladder pattern of the coiled loops, and the distended colon is identified by its haustral markings and location. A radio-opaque enema may be used in colonic obstruction to locate the site and may give information concerning the type of lesion. Similar information can be obtained in small-bowel obstruction that is being treated by decompression with the Miller-Abbott tube by the injection of a small amount of a thin mixture of barium through the suction lumen. The opaque mixture is withdrawn by suction at the conclusion of the examination.

Symptoms and signs vary in severity and in order with the site of the obstruction. High obstruction produces symptoms earlier and of greater severity, with nausea and vomiting predominating and distention less marked. Constipation appears only late, and evacuations may occur from the bowel below the obstruction for several days. Low obstruction produces a reversal of this order, with constipation as the usual presenting complaint, distention very marked, and nausea and vomiting appearing late.

The one phase of diagnosis that has become increasingly important is the recognition of strangulation. When all cases of obstruction were operated on, the recognition of strangulation was of academic interest. Now, however, when oper-

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ation may be delayed for days or weeks, its presence is of the utmost importance.

Obviously, there can be no rule for the diagnosis of strangulation, and a complete discussion of the problem involves the differential diagnosis of the acute abdomen. However, a few points must be mentioned. Lesions associated with circulatory interference, such as incarcerated hernia, intussusception and mesenteric thrombosis, must be considered at once and ruled in or out, so far as possible, by the history and physical examination. The patient with a strangulated bowel usually appears more toxic, and the leukocyte count is elevated above that expected in simple obstruction. A progression of the signs and symptoms over a short period of time strongly suggests circulatory embarrassment of the bowel. Tenderness on palpation localized in a small area of the abdomen and the palpation or demonstration by x-ray of an isolated loop of distended bowel are suggestive of a strangulated bowel. Persistent pain between the typical attacks of colic is usually on an ischemic basis. Abbott⁸ also mentions that small doses of morphine sulfate usually relieve the pain of simple obstruction but not that of strangulated bowel.

Distention of the bowel may result from an obstruction of its lumen or from paralysis of its wall. In the mechanical group, external hernias account for about 44 per cent of cases.⁹ Adhesions cause 31 per cent, and these may be subdivided into 13 per cent as a late postoperative complication, 11 per cent as an early postoperative complication and 7 per cent where no operation is involved. Neoplasms account for 9 per cent of cases, intussusception 5 per cent, volvulus 4 per cent, mesenteric thrombosis 3 per cent, gallstones 2 per cent, internal hernias 1 per cent and diverticula 1 per cent. The paralytic type of distention is usually preceded by peritonitis, acute infection elsewhere in the body or shocking injury. The two groups frequently merge. In any case, the normal emptying mechanism of the bowel fails and this initiates the pathologic physiology that is always the same.

The first effect of obstruction is the halting of the fecal stream, with an accumulation of the oral intake and of the secretions of the bowel, liver, gall bladder and pancreas above the point of obstruction. The secretions of the bowel itself are increased by the stimulus of the early distention. Gases next appear, and their presence is one of the first demonstrable signs of disordered function. They are chiefly swallowed air and carbon dioxide, with gases produced by fermentation playing a lesser role. The absorption of intestinal gas depends chiefly on the gradient between the

partial pressure in the vessels of the bowel and that in the inspired air. Thus, carbon dioxide is ordinarily quickly absorbed, whereas swallowed air must be expelled. It is apparent that swallowed air becomes the significant gas in the production of distention in the obstructed bowel. Wangenstein¹⁰ demonstrated this clearly when he showed that dogs with a complete obstruction of the bowel, but also with an occluded esophagus, do not become distended.

As the distention from the fluid and gases progresses, first the veins and the arterioles are compressed against the muscularis, thus producing edema of the bowel with a resultant loss of absorptive power. With the cellular breakdown of the mucosa the bowel becomes a simple osmotic membrane and more intracellular fluid is drawn into the lumen. Thus a vicious cycle is instituted that, if untreated, progresses until the vascular supply of the bowel is destroyed and gangrene and death ensue. The vague toxic factor is probably the result of products of bacterial invasion and protein breakdown after interference with the blood supply has occurred.

The motor effect of the distention is accelerated peristalsis initially with a progressive reduction thereafter. As the diameter of the intestine increases, the efficiency of peristalsis increases also. The volume of the contents is greater and thus the amplitude of each wave is increased. This is true until the distention reaches the point of interfering with the circulation, when motor activity diminishes and is finally abolished. There is a wide difference between the blood supply needed to maintain activity and that needed to support the life of the muscle, as is indicated by the prompt restoration of intrinsic activity by decompression of the bowel. The nausea and vomiting that occur are the result of a reversal of the fecal stream and not of a reversal of peristalsis. Regurgitant waves of peristalsis do occur proximal to the mid-duodenum but not distal to that point. As the dilatation of the bowel progresses beyond the point of maximum efficiency, a wave progressing caudally creates a current within the lumen in the opposite direction.¹¹

The results of these changes are easily seen. Dehydration appears rapidly owing to the lack of intake, the loss of fluid by vomiting and the outpouring of tissue fluid into the bowel lumen, where it is lost to the organism just as if it were outside the body. With the fluid depletion there is a large loss of chlorides. If the obstruction is high and the patient is vomiting frequently, the loss is chiefly hydrochloric acid from the stomach, and alkalosis may rapidly appear. If the distention is low, the loss is chiefly sodium

the reduction of total base may precipitate acidosis. The salt loss in the fluid within the bowel is approximately 6 gm. per liter. A severe and rapid hypoproteinemia also develops in these cases. The cause is not well understood, but is probably the loss of protein through the damaged mucosa, roughly similar to the loss through a damaged kidney. The vitamin stores are rapidly depleted and a state of acute malnutrition and vitamin deficiency appears.

Exact information concerning the metabolic state can be obtained with certain laboratory data—serum protein, bicarbonate and chloride levels and the hematocrit.

TREATMENT

An excellent rule of treatment is laid down by Abbott. In any case of intestinal obstruction, he says, the decision is not whether it should be treated medically or surgically but whether it should be treated medically or surgically at that particular time. This is a decision that must be reached at each visit to the bedside.

Treatment is directed at correcting the results of the obstruction, and as long as this can be accomplished the cause is of little importance. The relief of the distention is the prime consideration, and while this is being attempted, measures to restore the metabolic balance can be initiated. The last step is to effect the proper nutrition of the patient and replace the vitamin supply.

In discussing treatment the situations requiring immediate surgery will be omitted. These include the cases in which there is evidence of strangulation. They also include early mechanical obstruction, by which is meant those cases seen within the first twenty-four hours in which the cause of the obstruction is obvious, such as an external hernia. Left-sided colonic lesions, as a rule, warrant immediate surgery. In the last type of case, the slow development of symptoms tempts one to delay and decompress by medical means. However, unless the ileocecal valve becomes incompetent and small-bowel distention is present, the results by tubal decompression are poor.

Generally speaking, delayed operation is indicated in cases seen after the first twenty-four hours in which distention and dehydration are present. Right-sided colonic lesions may usually be delayed, since the small bowel can readily be decompressed and utilized to a point approximating the site of obstruction. Early operation should never be done in paralytic ileus, and probably never in intermittent obstruction in patients who have had several abdominal operations. The latter cases are almost invariably a combination of slight angulation with local edema and spasm,

and decompression usually relieves the obstruction. They are always subject to recurrence, but less so than if another laparotomy is performed.

It is in the paralytic group that medical management reaches its peak. This problem usually arises in peritonitis and pelvic abscess and following abdominal surgery. It is extremely gratifying to see an acutely ill patient with peritonitis and intestinal obstruction following a ruptured appendix begin to take a reasonable diet within a few hours after intubation and in a few days begin to have normal bowel movements. It is this type of case in which another operation would be extremely hazardous that operation may be avoided or delayed by medical decompression until the patient has been restored to a normal physiologic state.

Once it has been determined that a case is suitable for medical management, attempts must be made to adjust the disturbed electrolytes and relieve the dehydration. The first concern is the hypoproteinemia, which is rather extreme and accounts for a good deal of the edema of the bowel at the site of obstruction.

Partial obstruction may readily be converted into a complete obstruction on the basis of low-protein edema. Plasma or whole blood should therefore be given these patients early and as often as necessary.

Initially the usual fluid requirement is at least 3 liters. The necessary composition of this fluid varies but at first can safely be physiologic saline solution. After the first twenty-four to forty-eight hours the amount of salt given should be carefully calculated from the visible fluid loss, estimated invisible loss and blood-chloride determination. Once the hypochloremia is corrected, an excess of salt may lead to retention of fluid and may actually increase the obstruction. When laboratory data are available, the amount and type of fluid can be more intelligently estimated. Sodium lactate solution may be given to correct an acidosis, and more blood may be given if the proteins remain low. The hematocrit and the specific gravity of the blood are reliable indicators of the total amount of fluid. Five per cent glucose added to the salt solution or in distilled water begins the nutritional improvement.

When the intravenous therapy is under way, attention must be turned to the distention. Expulsion of the bowel contents depends on a functioning bowel wall and an avenue of exit. In any type of obstruction, except early partial obstruction or early paralytic ileus with some motor activity still present, there is no possibility of utilizing the normal route of exit. In these exceptional cases good results may be obtained by using

drugs, hot packs, enemas and rectal tubes. Morphine is frequently employed and is very popular. Probably its only function is to make the patient temporarily comfortable and reduce aerophagia. Its action is an initial duodenal spasm followed by a general relaxation of the small bowel that may last two or three hours.¹² Pitressin may be effectively used in a small group of cases. Its action varies at different levels of the bowel, but the end result is invariably an increase in the forward propulsion of the intestinal contents.¹³ Inhalation of 98 per cent oxygen may be of some help by increasing the gradient of gaseous exchange to aid in the absorption of swallowed air. Obviously it is of no use when the absorptive surface has been damaged.

The most obvious and successful method of relieving the distention is the actual removal of the fluid and gas by suction. Wangenstein⁵ recognized this and used gastric and duodenal suction in the treatment of these cases. With the development of intestinal intubation by Miller and Abbott¹⁴ in 1934 and the application of this principle in obstruction by Abbott and Johnston,⁷ an even more effective method was placed within reach. This procedure depends on the ability of the obstructed intestine to propel a large bolus, in contrast to its inability to pass a small one, and the restoration of muscular activity by decompression of the distended bowel. Two tubes are necessary or a tube with two lumens, one connecting with a distensible rubber balloon and the other available for aspirating intestinal contents. If such a tube is placed in the distal duodenum, the balloon inflated, and suction applied, it will proceed to the point of obstruction, or in the paralytic type will be expelled by rectum. As each segment of bowel is decompressed, its motor activity returns and the tube is carried to the adjoining segment. This method has many advantages. The loss of fluid into the bowel lumen can be accurately measured and a like volume replaced. The obstructive lesion can be definitely located and in many cases its nature can be determined. It is possible to feed the patient, withdraw the residue, and thus maintain nutrition over an almost indefinite period of time. The last makes the time of operation, if at all necessary, largely elective. As the tube advances the patient may be fed, progressively, clear fluids without milk, hard toast, cream cheese, junkets, jellies, custards, coffee, sugar butter, hard boiled eggs, rice, pureed vegetables and ground meat. It is a simple matter to have the patient receive 1500 calories daily on such a low residue diet. Vitamin B complex and 75 to 100 mg daily of vitamin C are added, and enteric coated salt tablets may be given to supply at least 5 gm for each liter of intestinal contents removed.

Technic of Intubation

The technical difficulty encountered by many in passing the tube has been the greatest objection to this method of decompression. It is true that the procedure is time consuming and works a good deal better in the hands of a person who has had adequate training in its use. Also, there

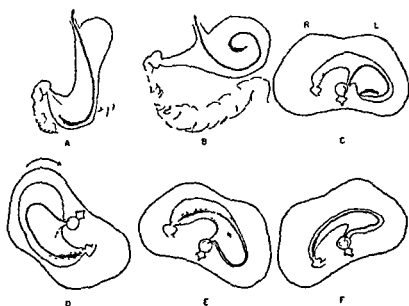


FIGURE 1 Intubation Technic

A shows the usual course of the tube in the stomach of a healthy subject and B, the change in the shape of the stomach and the resultant course of the tube in an obstructed patient. C represents a cross section at the pyloric level showing coiling of the tube in the fundus. D indicates the proper position of the patient during the injection of 300 cc of air into the stomach; the tube then drops to the pylorus but aspiration of the air allows the stomach to contract about the tube (dotted lines) and cut off the suction. E shows the direction in which to roll the patient to cause the air in the fundus to shift into a position from which it can be aspirated; the patient should never be rotated in the opposite direction since the tip will drop out of the pylorus. F indicates the position in which the patient should rest after the stomach has been emptied.

has been some misunderstanding concerning the time involved in placing the tube in the small bowel.

Placing a tube in the stomach is always justified in any circumstance in which immediate operation is not indicated. If after an hour or two of gastric decompression the patient is improving, a longer wait is justified. It may be six to twelve hours before the tube passes into the small bowel but so long as there is clinical evidence of improvement, both subjectively and objectively one may wait longer. Operation may, however, be indicated at any time during the course of intubation, and this is a problem that requires nice clinical judgment.

The Miller-Abbott tube is double barreled and the two lumens are separated by a thin rubber partition. One lumen connects with a rubber balloon and the other is available for suction.

the tip and openings proximal to the balloon. The tube is marked at the 60-cm. and 75-cm. levels from the tip and at 15-cm. levels thereafter.

The first step is to anesthetize the nose, which is done with a long cotton swab soaked with 2

lubricated with a water-soluble gel. The swab is removed from the nose, and the tube is passed into the stomach. Suction is applied and the stomach emptied.

The patient is placed on his right side and the

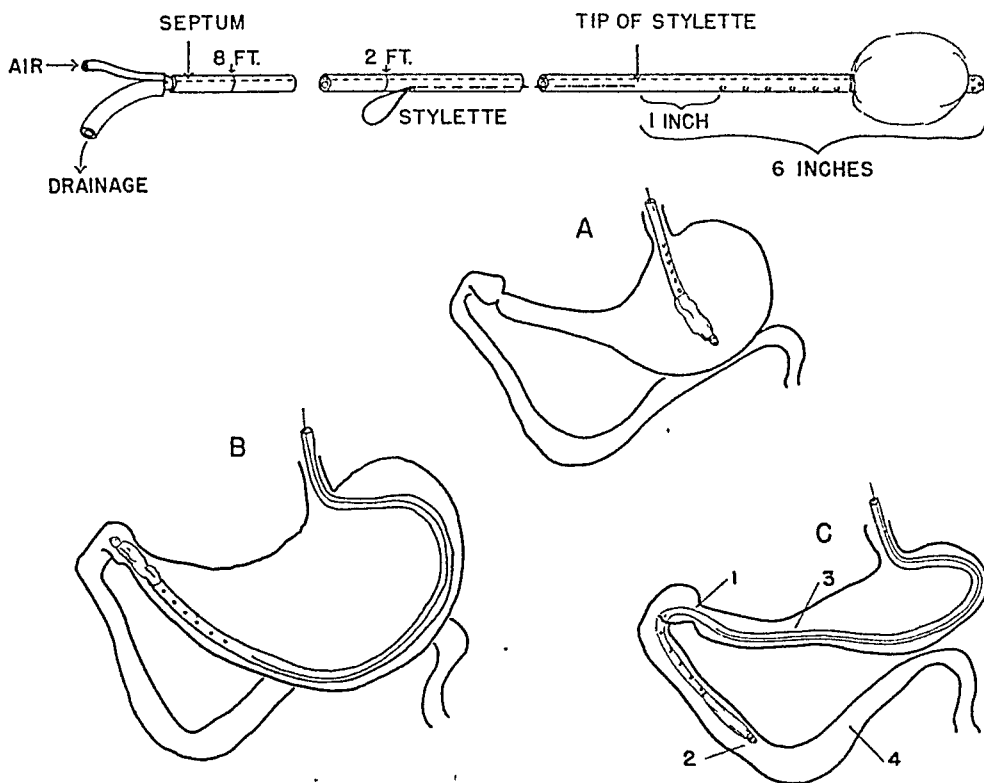


FIGURE 2. *Technic of Using a Stylet in Passing a Miller-Abbott Tube (Abbott¹⁵).*

Pierce the wall of the aspirating lumen of the tube at the 50-cm. (2-ft.) mark with a length of 0.4-mm. (0.016-in.), specially straightened, stainless steel vom Hofe leader wire, and advance the tip of the wire to a point 2.5 cm. (1 in.) above the most proximal aspirating hole in the tube. Bend a loop in the other end of the wire so that the tip cannot advance distally. The terminal 15 cm. (6 in.) of the Miller-Abbott tube will then contain no wire. Pass the tube in the usual manner to the position shown in A. With a temporary adhesive-tape patch over the point at which the stylet pierces the tube wall, inject 300 cc. of air into the stomach and advance the tube until it lies along the greater curvature, as in B. Hold the tube at the patient's nose to prevent its slipping out, and apply suction to remove the air. The stomach contracts, as in C, squeezing the tip of the tube ahead from position 1 to 2. The tip of the stylet then lies at 1. The antral spasm, with concentric contraction distal to 3, prevents the terminal 15 cm. (6 in.) from coiling, and the stylet prevents coiling of the tube proximal to the antrum, where the stomach is more flaccid. Draw back the tip of the stylet from 1 to 3, and by gentle, steady pressure on the tube at the nose advance the tip from 2 to 4. Withdraw the stylet, patch the hole through which it was introduced with thin rubber and, having inflated the balloon with 20 cc. of air, proceed as usual.

per cent Pontocaine. This is passed through the nares until its tip rests on the posterior pharyngeal wall. While this is left in place the tube should be tested for leaks or obstructions, and the amount of air necessary for the desired inflation of the balloon should be noted. The tube is then well

stomach is distended with 200 to 300 cc. of air. This step is necessary because of the reflex contraction of the antrum of the stomach found in cases of intestinal obstruction. The contraction converts the distal stomach into a narrow muscular organ and leaves a distended fundus into which

the tube readily coils. Distention of the stomach with air irons out the antral contraction and allows passage of the tube along the greater curvature to the pylorus. Reference to Figure 1 will make this clear. Enough slack is placed in the stomach to allow the tip to penetrate well into the duodenum. The patient is left in this position, suction is maintained, and clear fluids without milk are allowed until the tip passes into the duodenum. This is most readily identified by injecting air into the balloon. If the balloon distends with little or no resistance, it is in the stomach. A strong, steady resistance means that the balloon is at the pylorus. The resistance in the duodenum comes and goes irregularly, independent of respirations. When this desired resistance is noted, more tubing (several centimeters) is passed through the nose. After a fifteen-minute wait, the desired amount of air is injected into the balloon and the inflation tip is clamped. The tube is then passed at the rate of about 15 cm. an hour. It is well to check the progress by daily x-ray films of the abdomen.

Frequently the time factor is important and passage of the tube under direct vision with the fluoroscope is desirable. The tube may often be placed in the duodenum within a few minutes by this method, following the same steps as above. Another recently developed aid in the rapid passage of the tube is the stylet technic of Abbott,¹² illustrated in Figure 2.

Several difficulties are frequently encountered in the passage of the tube. Duodenal spasm from an injection of morphine is a common obstacle. This usually wears off within an hour, and until such time as it disappears only gastric suction may be obtained. Occasionally reflex duodenal spasm is encountered, in which event nitroglycerin or gastric washes with a warm solution of sodium bicarbonate may be effective in reducing it. Solid food in the stomach will prevent the passage of the tube until removed. Ascites makes passage of the tube difficult and fluoroscopic aid or the use of the stylet is usually required. Multiple obstructions such as are seen in adhesive types of peritonitis account for the majority of complete failures.

Once the tube is in place, several steps may be taken for the comfort of the patient. The use of an anesthetic lubricant for the tube is advisable. Five-tenths per cent ephedrine in saline r. se drops will relieve the nasal edema. Hot saline gargles and throat lozenges will soothe the throat.

The suction lumen should be irrigated with 20 cc. of saline solution every two hours. Obstruction by particles of food is not common and can readily be removed by alternate suction and compression with a syringe. A coil of tube in the

stomach will occasionally kink the tube enough to close both lumens. This can be recognized by the inability to get air in and out of the balloon, as well as the cessation of drainage from the suction side. Withdrawing a small length of tubing from the nose will release the obstruction.

The tube may be left in place safely for many days and even weeks. The possibility of erosion of the posterior pharynx or esophagus must be kept in mind, however. I have never seen such an erosion and am inclined to agree with Abbott that it is probably produced by too rapid removal of the tube. The removal must be accomplished slowly and intermittently, since pleating of the intestine will occur. Considerable pressure may be exerted on the bowel wall in this manner. For the same reason, the tube should never be taped or held in a constant position while air is still in the balloon. The pressure of the pleated bowel in such a case has been known to cause multiple perforations.

SUMMARY

Intestinal obstruction without strangulation may not be a surgical emergency. Nonsurgical methods of decompression done in conjunction with surgery have reduced the mortality from 30 to 10 per cent or less.

Distention of the bowel is recognized as the factor initiating the physiologic and chemical changes that occur in intestinal obstruction. The intelligent use of intravenous fluids and transfusions is effective in combating these changes temporarily.

Relief of the bowel distention is of primary importance and is best accomplished by intestinal intubation. The advantages of this method are several. Accurate measurement of fluid and electrolyte loss into the bowel lumen is possible. The obstructive lesion may be definitely located and in many cases its nature determined. Most important is the fact that, since the intubated patient may be fed a low-residue diet, nutrition may be maintained almost indefinitely, making the time of operation, if necessary at all, elective.

In any case of intestinal obstruction the decision is not whether it should be treated medically or surgically, but whether it should be treated medically or surgically at that particular time. This is a decision that must be reached at each visit to the patient.

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MEDICAL PROGRESS

ALIMENTARY-TRACT DISTURBANCES SECONDARY TO EMOTIONAL OR PHYSICAL TRAUMA

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DIGESTIVE disturbances incidental to occupational or traumatic episodes occur during the present war emergency with sufficient frequency to warrant clinical interest. Aside from their strictly medicolegal and industrial aspects, at the present time it may be of importance to enumerate and comment on the types of disorders that may be encountered as direct or indirect results of war conditions. Alterations in living and dietary habits, necessary limitations in articles of food imposed by war rationing and the stress and strain associated with the unusual degree of pressure existing today may well be expected to exaggerate and bring into sharp relief many of the alimentary disorders commonly encountered in normal civilian life.

Under ordinary circumstances, any survey of a given industrial group invariably reveals a serious loss of working hours because of so-called "functional disease." Thus a recent report by Bell,¹ of the Workmen's Compensation Board of Ontario, estimates the time lost from industrial injury due to functional disease as 20 per cent of the total—a tremendous figure. Much of this lost time might well have been saved, as Bell points out, by the proper treatment of patients and the education of the laity. In a single industry, Dignam,² for example, states that of fifty-eight claims, totaling 1754 days lost in one year, 20 per cent were due to disorders of the gastrointestinal system. Many of these difficulties are obviously due to poor work-

ing or living conditions associated with a given industry, fatigue, anxiety, faulty dietary habits and the like.

A more concrete picture can be obtained of the present situation by scrutinizing the numerous reports that have now begun to appear emanating from the military services of the countries at war. Early in the war it was noticed that indigestion appeared to present the greatest medical problem among the sick invalided home from the British Expeditionary Force in France. During the period between the dispatch of this unit to France and the end of April, 1940, one eighth of all sick men evacuated home had a primary diagnosis of gastric or duodenal disease, and of these more than 80 per cent showed gross organic disease, such as peptic ulcer of the stomach or duodenum. It is of interest that practically all subsequent reports have confirmed the original early statement of various English observers that the vast majority of men in military service complaining of gastrointestinal symptoms had such symptoms prior to induction into service.³ The incidence of ulcer in the British Expeditionary Force was in sharp contrast to figures obtained in the last war, where indigestion, inflammation and ulcers of the stomach were in a position somewhere between ninth and twelfth places in numerical importance. That this increase in gastrointestinal disturbances was not limited to the military services was evidenced by Willcox,⁴ who noted a striking incidence of digestive disorders in 1939 in London bus drivers. An interesting commentary by Mahlo⁵ in 1940 stated that soldiers in the German Army suffering from gastroduodenal ulcers lost their symptoms in

The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*. Volume III. 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5 00).

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the Polish campaign, while under the excitement and external emotional explosions incident to actual combat. He emphasized that these same soldiers when transferred to a quiet position on the western front suffered from a reappearance of ulcer symptoms.

Graham,⁴ in 1941, commented on the striking incidence of gastrointestinal complaints in military hospitals, the percentage of digestive disorders in two hospitals totaling about one third of the entire number of admissions. In these hospitals, where cases had been sent for diagnostic study, two thirds of the patients, who were drawn from the British Navy, Army, Air Force and women's auxiliary services, had ulcers. The ratio of duodenal ulcer to gastric ulcer was approximately 5:1, but other authors have reported a greater incidence of gastric lesions. In the British Navy, Allison and Thomas⁷ also point out the disproportionate rise in the incidence of gastric and duodenal ulcers, and again the point is made that less than 10 per cent of all subjects with ulcer develop their initial symptoms after entry into military service. The majority of writers have agreed that the most significant contributing factors are lack of a suitable diet and psychologic disturbances incident to military service. Frequently symptoms that have been controlled under conditions of civilian life reappear when men are forced to live on unregulated diets and are placed on active duty. A report by Wade,⁸ also based on observations made in the British Navy, notes that, during the first year of the war, relief of symptoms in patients with long standing histories of peptic ulcer was not possible while they remained on active duty. In March, 1941, it was decided that men with proved ulcer and those with a recurrence of symptoms and a definite past history of gastro-duodenal operation, perforation or hematemesis were to be invalided from the service. The only exceptions were a few officers or keymen who could be used for limited duty. Of 1000 cases studied, it is of extreme interest to note that the incidence of "dyspepsia" among men in active service in the Navy, as compared with those in the reserves and 'hostilities only' personnel, was in the ratio of 1:4. Such a figure suggests the effects of stress and strain and abnormal living conditions incident to noncombat duty, as well as those encountered during actual fighting. In the group of 1000 patients who formed the basis of his study, it is of interest that 20 of those with ulcer had had symptoms before the age of fifteen, and as noted above, only about 10 per cent dated the onset of symptoms from entrance into the service. For comparison, a report of Chamberlin⁹ on conditions existing in the Army of the United

States is of interest. His figures represent the results of the weeding-out process in the Army, beginning with the first day of the draft in October, 1940. The statistics are based on admissions to the Lawson General Hospital in Atlanta, Georgia, and the Tilton General Hospital at Fort Dix, New Jersey. Between August, 1941, and May, 1942, of approximately 3500 admissions, half were classified as medical patients, and of these nearly one fifth had gastrointestinal complaints. A third of the patients suffering from digestive disorders had peptic ulcer, the ratio of duodenal ulcer to gastric ulcer being 32:1. As already noted, in Britain the incidence of gastric ulcer has apparently been much higher, although the discrepancy with Chamberlin's figures may be more apparent than real, inasmuch as facilities for adequate x-ray investigation in the British medical units were not entirely satisfactory. A more recent article by Flood¹⁰ on the ulcer problem as observed at Fort Meade, Maryland, is entirely in accord with that of Chamberlin and gives an equally high incidence of duodenal ulcer—71 cases out of a total of 73, the remaining 4 being gastric ulcer. A comment by Flood is particularly pertinent to the military situation as it exists at present. Under careful routine treatment, two thirds of the service group with active ulcers continued to have symptoms for a period greater than two weeks whereas in a group of 225 civilian ulcer patients previously treated by this author, similar treatment secured complete symptomatic relief in two thirds of the patients well within the two-week period.

An article by Riley¹¹ bears particularly on the effect of wartime conditions on the civilian population, especially under conditions of total warfare. He quotes figures from the Royal Victoria Infirmary in Newcastle. In 1939 there were 200 perforated peptic ulcers, in 1940, 222, and in 1941, 251. Although the effect of air raids was less obvious in Newcastle than in some other large British cities that were severely bombed, these figures undoubtedly represent the increased strain of living under intense war conditions. As Riley points out, real anxiety (not trivial cares) aggravates ulcer symptoms, and malnutrition probably plays a part, both factors being intensified by the war. In spite of the statements of the British government that the health of the nation is better than ever before he finds evidence that digestive disorders and perforations of peptic ulcers are on the increase. He advocates, whenever possible, shorter working hours and improved canteen facilities as aids in controlling these conditions.

Dunn¹² notes the marked increase in the figures for gastric disturbances encountered in the present war over those recorded during World

War I, and stresses the importance of emotional factors arising from the war situation. He suggests that the digestive disturbances growing out of the present emergency are those of psychosomatic disorders, in contrast to the neurotic manifestations (anxiety states and conversion hysteria) that were much more frequent in the last war. He states that the frequency of gastroduodenal disorders appears in part to be related to inadequate screening of recruits with a history of ulcer or with a markedly neurotic personality structure, and in part to prolonged tension in men mobilized for war but with little opportunity for the release of emotions in combatant activity, a thesis that would appear to have some confirmation from the opinions noted above.^{5, 8, 11}

To the effects of what may be called emotional trauma of the stress and strain of total war in producing alimentary-tract disorders may be added the results of physical trauma connected directly or indirectly with the conditions encountered in the present conflict. Acute ulcers of the stomach or duodenum, the so-called Curling's ulcer following extensive burns, have been known since they were originally described by Dupuytren in 1832. The total number of such ulcers recorded in the literature is surprisingly small. Until 1938, approximately 110 cases of such acute ulceration following cutaneous burns were to be found in the literature. An excellent case description and a complete survey of the entire literature on the subject are to be found in an article by Keely.¹³ In his case, vomiting occurred on the fourth and sixth hospital days, and at this time fluoroscopic examination revealed a duodenal deformity, although there had been no preceding gastrointestinal symptoms. Although Tenery¹⁴ was able to show no marked changes in the blood-electrolyte pattern in patients suffering from extensive cutaneous burns, his report of the autopsy findings in one of his 3 fatal cases is of interest in that it showed a mild, terminal, diffuse hemorrhagic gastritis. Curling's original description included ulcers of the duodenum only, associated with "violent congestion, severe gastroenteritis and more or less vivid red patches and deep ulceration." In Tenery's 3 fatal cases, it is of interest to note that all showed marked liver changes. An experimental investigation of Necheles and Olson¹⁵ represents one of the most valuable contributions to an understanding of this particular type of gastrointestinal trauma. These authors noted the effect of cutaneous burns on gastrointestinal secretion and motility. It was known that following shock of any kind, petechial hemorrhages, congestion of the mucous membrane and erosions or superficial ulcers may be found in the stomach, duodenum or intestinal tract. Necheles and Olson found

that in anesthetized dogs extensive burns were associated with a diminution of the salivary, biliary and pancreatic secretions. Gastric secretion and gastric acidity increased in a number of experiments, and in one animal a fresh prepyloric ulcer was found. A considerable increase was noted in intra-abdominal pressure and in gastric motility. The increase in motility was particularly noticeable in the pyloric antrum and began immediately after burning had occurred. The authors believe that these findings throw some light on the pathogenesis of Curling's ulcer. Although this type of ulcer becomes clinically apparent only after a considerable delay following the burn, it can be assumed that the local acute disease begins to develop at a much earlier date.

In this connection, it is of interest to comment on the findings noted among some of the victims of the recent Coconut Grove disaster.* Although none of the patients admitted to the Massachusetts General Hospital had symptoms of ulcer, 56 per cent of those whose stools were examined showed evidence of bleeding. The reports of 3 cases that came to autopsy are of interest. In one person, who was dead on arrival at the hospital, the entire length of the duodenum showed extensive submucosal hemorrhage, which was dark pink in color and took the form of circular streaks following the lines of the mucosal folds. The jejunum was negative, but the last 25 cm. of the ileum showed extensive submucosal hemorrhages, which were not so severe as those noted in the duodenum. Microscopic examination of the duodenum revealed that the vessels of the mucosa and submucosa were maximally dilated and formed the scattered petechial hemorrhages noted in the mucosa. In the other patients, dying fifty-three hours and sixty-three hours after the disaster, marked injection or minute petechiae were noted in the mucosa of the duodenum. In addition, numerous red, punctate areas, ranging from 0.5 to 5.0 mm. in diameter, were noted in the gastric mucosa. They were more frequent near the cardiac end of the stomach. No true erosions were found. Because of the high incidence of serious burns associated with modern warfare, it is obvious that these findings are significant.

Although not implicated in the hazards of total warfare, mention should be made of intestinal injury as a result of intensive radiation to neighboring structures. This has been commented on by various observers, but its importance cannot be overestimated because of the crippling and dangerous sequelae that may follow heavy irradiation, particularly that of pelvic tumors. A complete study of the pathologic changes occurring in radiation lesions in the gastrointestinal tract has been

*Management of the Coconut Grove burns at the Massachusetts General Hospital. *Ann. Surg.* (in press).

made by Warren and Friedman.¹⁶ Thirty-eight cases were selected, including ulcers, fistulas and strictures, many of which developed at sites distant from neoplastic tissue, but some of which occurred at the site of a partially or completely destroyed tumor. The bowel wall was usually thickened and indurated, with an opaque serosa and prominent telangiectasia. Similar mesenteric changes were also noted. The bowel mucosa was the seat of frequent superficial to deep ulcerations, with at times pronounced necrosis and massive gangrene. Stenosis was sometimes due to diffuse sclerosis with general constriction of a segment. Experimental observations on rabbits by the same authors¹⁷ confirmed the identity of the experimental lesions with those noted after clinical radiation. That such lesions may occasionally cause a perforation of the intestine is indicated in a report by Parks¹⁸ of a case in which the adjacent sigmoid became ulcerated and necrotic following radiation of the cervix for a squamous-cell cancer. In this connection, it is of some interest to point out the observations made by K'O, Tu and Chan.¹⁹ who were interested in the possible unfavorable effects that might occur with the administration of iron during irradiation therapy. In animal experiments, it was found that ferrous sulfate was definitely valuable in the treatment of anemia as a result of chronic blood loss and caused no harmful effects in the animals undergoing irradiation. When ferrous citrate was given under similar circumstances, radiation of the abdomen was associated with gross intestinal lesions similar to those described by Warren and Friedman.

Direct injury to the gastrointestinal tract may be caused by the ingestion of irritating substances or of foreign bodies, by the trauma incident to endoscopic examination for diagnostic purposes, by penetration associated with therapeutic measures applied to neighboring organs or by other means. The injury to the buccal, esophageal and gastric mucous membrane following the ingestion of lye and similar substances owing to their direct caustic action is well known, as is the effect of swallowing foreign bodies, such as fishbones. In the case of foreign bodies, including bone spicules, wood splinters, pins and the like, the commonest sequel is that of intestinal perforation involving the lower ileum and cecum. Not infrequently perforation occurs in the appendix or in a Meckel's diverticulum. The incidence of such lesions and the variations encountered are thoroughly discussed by MacManus²⁰ and by Bunch and his associates.²¹ Some unusual cases of this character are recorded by Hill,²² who reports 4 cases of traumatic hemorrhage of the intestinal tract occurring on board an American naval vessel. In each

case, the illness was characterized by the sudden onset of dizziness, weakness and collapse, without a recognized cause. Eventually an explanation was obtained in the discovery of small, sharp pieces of tin in the food served to the sailors. At the same time, a defective can opener was discovered that dropped bits of metal into the food. Discovery of the cause was delayed because of the poor lighting incident to numerous blackouts on the ship. A somewhat similar and obscure cause of hematemesis is found in a report by Bannister.²³ The point of particular interest is the fact that the foreign bodies, which in this case were ordinary steel needles, were found in the pancreas, the splenic artery and the hepatic end of the transverse colon, to which they had penetrated by perforating the duodenum. An important recent cause for gastric irritation directly associated with the war is cadmium, a metal recently used instead of tin and other valuable war metals to plate cooking utensils. Although cognizance has been taken by some public-health agencies of this form of food poisoning, which results in violent, acute gastritis, it is important to recognize that cadmium plating of food utensils may be encountered and may prove a source of serious poisoning. The danger results from the solubility of this metal plating in weak acids, such as acetic acid and other organic acids commonly found in food. Their action on the plating results in the formation of organic cadmium salts that are extremely toxic when combined with the hydrochloric acid of the gastric juice. The report of Frant and Kleeman²⁴ covers adequately this particular hazard to the gastrointestinal tract.

Actual rupture of the stomach following the ingestion of common substances, such as soda bicarbonate, may occur. Such a case is reported by Lemmon and Paschal,²⁵ and although the occurrence is not frequent, their report is of interest. The patient, after taking several drinks and a heavy meal, took a large dose of bicarbonate of soda to relieve the heavy feeling in his stomach. This was immediately followed by sudden, severe, generalized abdominal pain with subsequent shock. Death resulted from toxemia and peritonitis following rupture of the viscus.

Because of the frequent use of endoscopy as a diagnostic aid, it is pertinent to mention the dangers inherent in the various endoscopic methods employed. The necessity for these measures is obviously not dependent on the war, but the need for them will undoubtedly be increased because of various digestive-tract disturbances incident to industrial and war conditions. The diagnostic value of peritoneoscopy is well established, particularly in evaluating obscure hepatic disorders

and pelvic tumors. In spite of the fact that the number of serious accidents is relatively few, peritoneoscopy does rarely result in perforation of the bowel in those cases where it is employed in the presence of a plastic peritonitis that has not previously been suspected. The difficulty that exists at times in differentiating between ascites and distended, fixed loops of bowel is such that similar accidents are not altogether avoidable, but the risk entailed in the use of this procedure must be understood and accepted. Ruddock,²⁶ Benedict,²⁷ Thieme²⁸ and Garrey²⁹ report only minor accidents in the use of the peritoneoscope, and in a more recent survey Benedict³⁰ has encountered, in an attempt to diagnose extremely obscure cases, only 4 cases out of a total of nearly 500 peritoneoscopies in which unavoidable penetration of the intestine followed the use of the instrument. Several years ago Schindler³¹ surveyed the results of over 22,000 gastroscopies performed by sixty examiners and found 1 fatal accident resulting from perforation of the hypopharynx. Nine other cases with complications, which were not fatal, were reported, 8 of them having perforation of the gastric wall and 1 perforation of the jejunum. In 5 cases, perforations of the stomach could be attributed to the friction of a rubber-sponge tip, which has now been discarded. All the gastric perforations were found in the upper portion of the posterior wall of the stomach. Schiff and Shapiro³² reported 3 accidents following 1300 gastroscopies, 1 of which was presumptive and 2 were proved. In the proved cases, perforation occurred at the time the instrument was introduced and produced no immediate pain. As noted by Schindler, the perforations were high on the posterior wall of the stomach. One of these patients died seventy-two hours after the accident. Schindler states that a diagnosis of gastric perforation at gastroscopy may be made prior to the onset of pain if the stomach remains collapsed in spite of air inflation. An additional case is that reported by Touroff,³³ whose patient suffered a perforation of the cervical portion of the esophagus with a flexible gastroscope. Perforation was immediately diagnosed by the appearance of a small amount of blood in the mouth when only a portion of the instrument had been introduced, although without apparent difficulty. The instrument was immediately withdrawn, and a few moments later the patient began to complain of pain in the right side of the neck, with associated tenderness and crepitation. In spite of this accident, the patient survived and is now well. Because of the fact that esophagoscopy is usually performed in the presence of serious disease, such as carcinoma, it is to be expected that occasional ac-

cidents may be encountered even when the most careful technic is employed. Benedict³⁴ reports 6 cases of perforation, in only 1 of which it was fatal, in the course of esophagoscopies performed on 340 patients. Similar penetrating lesions of the rectum and sigmoid have been produced by sigmoidoscopy, with or without inflation and with or without the attendant use of a biopsy forceps. Although serious danger to the alimentary tract incident to the use of endoscopic methods is not great, it must be emphasized that in the presence of disease processes the greatest care should be used and manipulation should be done only under the most favorable circumstances.

A somewhat similar hazard is occasionally encountered in uterine curettage; however, fatalities due to perforation of the uterus and the neighboring bowel are, fortunately, rare when the operative procedure is carried out by a competent person. Probably the most frequent source of such a danger is associated with criminal abortion, frequently with fatal results. Numerous reports can be found in the literature, but the subject is sufficiently well recognized to require no further comment.

Rupture of the colon by compressed air is an unfortunate but not uncommon accident. The rupture is produced by a jet of compressed air that readily passes through cloth and enters the anus, even when the jet is not accurately directed at it. Such a gaseous jet is elastic and expands in all directions, adapting itself to surroundings. Perforation occurs usually at the rectosigmoid angle. Rarely the serous and muscular coats of the bowel only are torn. A diagnosis may be made on the basis of the history alone or on physical signs, the most important of which are the presence of abdominal distention, the absence of liver dullness and embarrassed respiration. Brown and Dwinnelle³⁵ report 3 such cases and review 6 others found in the literature.

Damage to the stomach or bowel by penetrating injuries is not new, and represents a not uncommon type of accident encountered in civilian life. It is of particular significance at the present moment because of the obvious danger from such penetrating wounds as may occur in war injuries due to bayonet, bullet and shell fragments, and also to penetration of the hollow viscera resulting from a fall from a considerable height and impalement on a sharp object. Even where multiple lacerations of the digestive tract have resulted, with modern methods of surgery and the timely use of the sulfonamides many favorable recoveries may be expected.³⁶

Of less obvious but equally great significance are the indirect injuries to the gastrointestinal tract

resulting from nonpenetrating trauma. Prior to the war, numerous cases of perforation of the digestive tract at various levels following such trauma have been recorded. Such perforations have resulted from automobile and industrial accidents, kicks from animals and so forth. The esophagus has only rarely been ruptured following a blow on the abdomen,—a case is reported by Aldrich and Anspach,³⁷—but perforations of the duodenum, jejunum and intestinal tract are not uncommon. Counseller and McCormack³⁸ reviewed the literature and state that in subcutaneous abdominal injury the small intestine was the site of rupture in 90 per cent of reported cases, the jejunum and ileum equally forming together 80 per cent of the entire group. Such accidents occur more frequently in adults than in infants and children, although the latter have occasionally suffered such trauma when heavy objects fell on the abdomen. Frost and Guy³⁹ report retroperitoneal perforations of the duodenum, without other intra-abdominal injury, in an adult who fell on the right side, striking the right upper quadrant of the abdominal wall against a blunt object. Poer and Woliver⁴⁰ studied the cause of injury in nearly 1500 cases and showed that many of the injuries were produced by a relatively slight blow to the abdomen. These authors point out that the extreme fragility of the intestine was known to Aristotle, and quote him as saying that "a slight blow will cause rupture to the intestine without injury to the skin." Three chief mechanisms are mentioned that may result in intestinal and mesenteric injury due to nonpenetrating abdominal trauma: first and most frequent, a crushing injury in which an external force compresses the bowel against the spine or pelvic bones; second, a tearing injury that may result from a violent force applied at a tangent to the body; finally, severe bruising injuries that increase the normal pull on an organ. The existence of a hernia obviously may be a predisposing cause of a traumatic rupture of the intestine. A significant point is that distention of the intestine with food or fluid frequently contributes to the likelihood of rupture following a blow from a blunt object. From the medicolegal point of view, it is essential that symptoms shall appear immediately following trauma. That an existing peptic ulcer may be caused to bleed by trauma of this sort is not surprising, and such cases have been recorded by numerous observers. In relation to the present war, it is interesting to note that severe perforations or hemorrhages in ulcer patients have occurred during flight. Under flying conditions, it is conceivable that various factors may become operative, including anoxia, compression and trauma, such as may occur in airplane accidents or

from sudden diving at high speed with the subsequent pull-out, in addition to the more obvious effects of nervous strain and tension incidental to combat flying at high altitudes. Several interesting reports of this nature are to be found in the war literature.^{36, 41, 42}

Traumatic peptic ulcer falls into a different category, however, and not only has interesting medicolegal aspects as encountered in civilian life, but occasionally occurs during combat conditions. A sufficient number of cases have been recorded in recent years since Potain's original description of a traumatic ulcer in 1866 to make it highly probable that acute ulcers of the stomach or duodenum may occur solely as the result of sudden trauma. The question of the relation between trauma and peptic ulcer frequently arises in regard to accident insurance and workmen's compensation. The German State Insurance Office has denied that such a relation can exist. A history of trauma is obtained in not more than 2 per cent of all peptic ulcers, according to Kellogg and Kellogg,⁴³ who have reviewed the subject exhaustively. When trauma is claimed as the cause of ulcer, the implication usually holds that a blunt force directed to the epigastrium without direct penetration of abdominal and visceral parietes has resulted in variable degrees of injury to the epigastric wall and to the underlying viscera. Eusterman and Mayo⁴⁴ claim that external violence may be great enough to produce multiple acute gastric ulcers, or a less severe injury may be followed promptly by the onset of symptoms of a peptic ulcer that was previously nonexistent. They cite the four postulates of Liniger and Molinicus as the medicolegal considerations necessary to warrant compensation for traumatic ulcer. These are: adequate proof of absence of gastric disease before the accident; injury sufficient to cause the lesion and trauma localized in the epigastrium; symptoms that immediately follow the accident; and the continuation of symptoms and signs pointing to a gastric or duodenal ulcer. According to Guy,⁴⁵ who cites voluminous foreign literature, and a few American authors, in the majority of cases the trauma must be sufficient to cause some signs of hemorrhage into the lumen of the stomach or bowel. Although the medicolegal aspects of this particular problem are of the greatest interest, it is important to remember that traumatic ulcers are likely to occur, and a careful watch should be kept for such unusual findings in the present war. It seems likely that the acute trauma incident to mechanized warfare may well produce a fair number of such cases.

Another type of injury secondary to nonpenetrating abdominal trauma is not uncommonly en-

countered in civilian practice and is to be expected as a result of war injuries. This is traumatic diaphragmatic hernia following concussion or a severe blow to the abdomen by a hard object. Such herniations may occur on the right or left side of the diaphragm. With an already existing paraesophageal hernia, it is to be expected that such accidents will not be uncommon. Numerous cases were reported in the last war, either with or without penetrating wounds. Much more commonly one encounters traumatic inguinal hernias, which frequently form the basis of long and costly litigation in relation to industrial medicine and workmen's-compensation cases.

A much more controversial subject is traumatic appendicitis. A large number of such cases have been reported in the literature as a result of severe falls or blows involving the abdominal wall. The forces necessary to cause traumatic medicolegal appendicitis apparently may be internal, external or both combined. As in traumatic ulcer, certain postulates are necessary for this diagnosis, and Shutkin and Wetzler⁴⁶ outline the following: there must be absolute freedom from complaints of nausea, vomiting or abdominal tenderness preceding trauma; direct trauma must be severe and forcible involving directly the abdominal wall, especially the right half; indirect trauma (from a fall or strain) must be violent, acute and unexpected; symptoms must appear immediately after trauma, indicating localization in the right lower quadrant of the abdomen; symptoms must be persistent and progressive and must assume the clinical symptoms and signs of clinical appendicitis; the pathological examination of the appendix must indicate a suppurative, destructive and necrotic process. Compensation for traumatic appendicitis has been awarded in numerous courts in cases in which rupture or damage to the appendix with perforation has been found following an accident. Traumatic appendicitis, however interesting, must be extremely rare, and such a diagnosis is tenable only after an extremely careful review of all the facts. I have recently heard of one highly suggestive case of this condition. A previously healthy young adult experienced a sudden onset of abdominal pain immediately after an airplane dive at high speed. Emergency operation revealed an acute perforated appendix. If such a case can be accepted as an authentic example, it is probable that this also constitutes one of the rare hazards of war aviation.

Of greater numerical importance and of greater interest at the present moment are the concussion injuries to the gastrointestinal tract resulting from blasting or bombing. Such injuries are particularly well described in excellent and comprehen-

sive articles by Gordon-Taylor³⁶ and by Breden and his associates.⁴⁷ Although the abdominal viscera appear to be less sensitive to blasts than are the lungs, any portion of the gastrointestinal tract may exhibit pathologic changes consisting of hemorrhage, varying from punctiform spots under the serosa to large annular extravasations, and occasionally rupture of the bowel. The proclivity of the small bowel to exhibit lesions due to blasts is not much less than that of the large bowel; the stomach is seldom affected. Extensive blood infiltration of the mesentery with extension under the serous coat of the bowel has also been noted. Paralytic ileus has been observed as an accompaniment of blast injuries to the abdomen. One of the striking results of nonpenetrating trauma to the abdominal cavity secondary to concussion is that of acute dilatation of the stomach. Gordon-Taylor mentions several such cases. It occasionally occurs some days after concussion and may have a fatal ending. A striking example of blast trauma may be noted, the result of a "near-miss" bomb. The patient entered the hospital in considerable abdominal pain, but examination revealed no external bruise or abrasion. Because of abdominal tenderness and rigidity, operation was performed, revealing a large subserous hematoma that had spread under the duodenum from the pyloric end of the stomach and had infiltrated into the layers of the transverse mesocolon. The various coats of the duodenum had become separated, requiring complete division. In passing, it may be pertinent to point out that under such circumstances abdominal rigidity does not of necessity betoken involvement of the subphrenic viscera. It is well known that injuries of the pleura or lung, especially if occurring in proximity to the diaphragm, may occasion abdominal rigidity and arouse suspicion of an abdominal lesion.

Extremely strenuous muscular effort may result in subparietal rupture of the intestinal tract. This is most frequently associated with a pre-existing hernia. The precipitating accident is frequently caused by the lifting of a heavy weight or pulling against great resistance. Many such cases have been reported by Wilensky and Kaufman⁴⁸ and by MacMillan.⁴⁹ Where noted, all perforations occurred at or near the antimesenteric border of the involved loop of bowel. Such a type of lesion has an obvious relation not only to war injuries but also to industrial accidents.

An unusual type of intestinal disturbance is that reported by Altemeier and Wadsworth,⁵⁰ who record intestinal ileus following a fracture of the ribs. A few such cases have been noted in the literature since the original report by Adams in 1910. Abdominal distention may appear within ten hours

after the injury or may be delayed for several days, and may last for as long as six days. If the possibility of a ruptured intra abdominal viscus can be ruled out, conservative therapy is indicated. The chief difficulty arises in the differential diagnosis between upper abdominal spasm secondary to an irritation at the lower end of the costal nerves caused by the fracture itself and an irritation of the dorsal sympathetic ganglions and splanchnic nerves with resulting dilatation of the small bowel. The latter, resulting from displacement of the head of a rib or proximal fragment, retropleural edema or hematoma in the upper vertebral area, seems to offer the most logical explanation of such a phenomenon.

SUMMARY

Various types of trauma directly or even fairly indirectly associated with the present period of excessive strain and stress are enumerated and discussed.

In view of the variety of traumatic episodes that may produce organic or functional digestive tract symptoms, attention is called to these important, although scattered, manifestations of gastrointestinal disease.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29191

PRESENTATION OF CASE

A sixty-seven-year-old man was referred to the hospital because of nausea and vomiting.

The patient apparently had been well until twelve days prior to admission, when he suddenly felt nauseated after breakfast and vomited thin fluid containing a few flecks of blood. The nausea and vomiting continued, particularly after ingesting solid foods, and he was able to retain only small amounts of milk, water and fruit juices. A gastrointestinal series two days before admission was said to have revealed pyloric obstruction. There was no further bleeding, and no jaundice, diarrhea, constipation, bloody, tarry or acholic stools or weight loss.

The patient's father had died of carcinoma of the stomach. The past history was noncontributory.

Physical examination disclosed a large, heavy-set man who seemed comfortable. The skin and mucous membranes were dry. The heart and lungs were normal. The abdomen was soft; no masses were felt, and no tenderness elicited.

The blood pressure was 100 systolic, 64 diastolic. The temperature was 97°F., the pulse 120, and the respirations 26.

Examination of the blood revealed a hemoglobin of 14 gm. and a white-cell count of 14,000, with 83 per cent neutrophils. The urine was acid, had a specific gravity of 1.016 and showed a + test for albumin; the sediment contained rare hyaline and granular casts and occasional red, white and epithelial cells. The stool was tan and was guaiac negative repeatedly. The blood sugar was 104 mg. per 100 cc., the protein 6.5 gm., the nonprotein nitrogen 104 mg., and the chloride 107.9 milliequiv. per liter. Five days later, after glucose-saline infusions, the nonprotein nitrogen was 30 mg. per 100 cc.

A barium meal passed rapidly through the esophagus; the mucosa appeared normal, and there was no evidence of esophageal varices. The stomach contained a considerable amount of gas and a small residue from a previous barium meal. Very little barium left the stomach during the ex-

amination. The mucosal pattern appeared normal. The stomach was rotated on its large axis so that the greater curvature pointed forward, and the pylorus and duodenum lay behind the antrum. Therefore a satisfactory examination of the pyloric sphincter and duodenal bulb was not obtained. In six hours the greater part of the barium mixture was still in the stomach and there was no barium visible in the small bowel. The colon was well filled from the previous barium meal and showed many large diverticula scattered along its course. The liver did not appear to be enlarged. A second barium meal yielded no additional information.

An operation was performed on the fifteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD B. BENEDICT: This is essentially a story of pyloric obstruction. The differential diagnosis seems to rest almost entirely on the causes of pyloric obstruction. There are one or two things in the history that might be mentioned. The patient's father died of carcinoma of the stomach. Some families have more cancer than others, but I do not believe one can put any weight on that. He had not lost weight, which is a little bit against carcinoma. The skin was dry; he was obviously dehydrated. That would go with the nonprotein nitrogen of 104 mg., which later became normal after saline infusions.

I shall take up the least likely things first. The first is volvulus, which is only suggested by the fact that the stomach was rotated. If he had volvulus causing pyloric obstruction, he should have had severe pain, tender epigastric swelling and probably more severe vomiting if the obstruction was at the cardiac orifice. That is not this picture at all. Adhesions around the pylorus cause partial obstruction, but I have never seen them cause complete obstruction of this sort. Pressure from extrinsic tumors can cause some pyloric obstruction, but I should not expect it to cause complete obstruction. Carcinoma of the pancreas occasionally invades the wall of the stomach and causes some obstruction, but, again, it is never complete. Gastritis is the commonest disease of the stomach, but I have never seen it cause complete pyloric obstruction.

The commonest causes of obstruction are tumor and ulcer, and of the tumors, cancer is much the commonest. We might consider lymphoma, leiomyoma, leiomyosarcoma and neurofibroma. These are tumors that, in my experience, do not cause complete pyloric obstruction. Benign tumors of the antrum can prolapse through the pylorus into the duodenum and cause partial obstruction. But

that is always intermittent, and the tumor should be easily seen by x-ray. So far as carcinoma goes, the patient is in the proper age group. I should not, however, expect the onset to be quite so sudden, with no preliminary symptoms and no anorexia. He did have some bleeding, which goes with either carcinoma or ulcer. He had had no weight loss. That is possibly against cancer, but the one big thing against cancer of the stomach is the x-ray picture, which showed a normal mucosal pattern, and there is nothing to indicate that the x-ray examination was unsatisfactory except that there was pyloric obstruction. The record does not state that there was fluid in the stomach to obscure the x-ray findings. Gastros-copy might have helped but was not done.

May we see the x-ray films?

DR. RICHARD SCHATZKI: We have films taken on three different dates. This is the preoperative film showing nothing more than the record stated—a stomach with normal mucosal folds so far as one can see them. The spot film shows the same thing. The greater part of the body is visible and appears to be normal. I cannot see the pylorus in any of these films.

DR. BENEDICT: Would you say the examination was unsatisfactory.

DR. SCHATZKI: I think that is impossible to say from the films. Apparently there was some fluid in the stomach but not too much. There is one spot film here that shows just at the tip, where one would expect the pylorus to come out, something that looks like a crater. From the films I have here, I cannot tell whether it is in the stomach, beyond the stomach or at the pylorus. It looks as if there might be a crater in that area, but from the films alone I cannot tell you what it is.

DR. BENEDICT: I am inclined to rule out a tumor of the stomach on the basis of the x-ray findings.

Then we come to ulcer. I have never seen ordinary gastric ulcer cause complete pyloric obstruction. Prepyloric ulcer should be seen by x-ray and should show narrowing of the prepyloric area and a crater. It does not ordinarily cause complete obstruction. An ulcer at the pylorus, which is classified as duodenal because such ulcers do not tend to become malignant and occur a little bit on the duodenal side, can cause complete obstruction after having been silent for many years; and this is often the first symptom. The patient was a little old for that to have occurred, but my feeling is that the most likely diagnosis is either a pyloric or a duodenal ulcer with obstruction.

DR. WILLIAM B. BREED: Could a polyp in the lower part of the stomach or a polyp of the duodenum, with which I am not familiar, have been present that did not show up on the x-ray film and might have caused pyloric obstruction?

DR. BENEDICT: I spoke of a polyp that had prolapsed through the pylorus; but I think that the symptoms would have been intermittent and that the lesion would have shown by x-ray.

DR. SCHATZKI: Inasmuch as we do not see the pylorus in these films it is difficult to discuss that, but I should expect that, with an obstructing polyp, one would have no trouble in demonstrating its surface, even if it had not intussuscepted.

DR. AUGUSTUS ROSE: Why was there no peristalsis in the stomach?

DR. BENEDICT: When there is complete obstruction, the wall gets atonic and peristalsis ceases.

DR. TRACY B. MALLORY: I am sorry Dr. McKittrick is not here to describe the operation and the subsequent course. I shall do the best I can from his notes.

It was decided to explore and do a jejunostomy at the same time. On going into the abdomen, Dr. McKittrick could feel a mass in the region of the first portion of the duodenum. He could not be perfectly sure whether or not it involved the stomach, but it definitely did involve the first portion of the duodenum. He eventually decided to do a gastroenterostomy, and because of certain technical difficulties resulting from a thick and fatty mesentery, it was necessary to do an anterior instead of a posterior gastroenterostomy. In addition to that an enteroenterostomy was done between the two loops of jejunum that were used for the gastroenterostomy. I might stop at that point.

With that description, Dr. Benedict, would you care to go any farther in discussing the probabilities?

DR. BENEDICT: I still think that the diagnosis of ulcer, with an inflammatory mass, is tenable.

DR. MALLORY: What would you say about carcinoma of the duodenum or extension of cancer of the stomach into the duodenum? The duodenum was definitely involved.

DR. BENEDICT: Cancer of the duodenum is extraordinarily rare. We have seen a few cases of cancer of the stomach extending into the duodenum; but a few years ago such a condition was considered to be impossible.

DR. MALLORY: It used to be a dictum in all surgical textbooks that cancer of the stomach never extended beyond the pylorus.

DR. BENEDICT: But you have seen a few cases.

DR. MALLORY: It does quite frequently, if one looks for it with a microscope. One does not often see gross extension, however.

DR. BENEDICT: I should not think that it was terribly likely with complete obstruction. Perhaps I am a bit stubborn, but I prefer to stick to ulcer with an inflammatory mass.

DR. MALLORY: That was Dr. McKittrick's impression at the end of the operation.

Following operation literally nothing happened. The stomach never emptied itself. The patient was kept under observation nearly three weeks more, vomiting daily in spite of gastric aspirations that frequently reached a liter a day. No fluid left the stomach either by the pylorus or the gastroenterostomy opening. Despite the use of drugs such as prostigmine and mecholyl, it was never possible to produce a peristaltic wave. Finally, a second operation was done and another enterostomy was performed a little lower down: For two weeks more nothing ever left the stomach and the patient finally developed minor pulmonary signs and faded slowly out of the picture.

CLINICAL DIAGNOSIS

Pyloric obstruction (? carcinoma or benign ulcer).

DR. BENEDICT'S DIAGNOSIS

Duodenal ulcer, with pyloric obstruction.

ANATOMICAL DIAGNOSES

Carcinoma of pylorus, infiltrating duodenum and mesentery.

Pyloric obstruction.

Gastric dilatation.

Operative wounds: anterior gastrojejunostomy, enteroenterostomies and jejunostomy.

Hemothorax, left.

Massive collapse, left lung.

Healed apical tuberculosis, bilateral.

Arteriosclerosis, generalized, moderate.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The post-mortem examination showed that there was a definite tumor in the region of the pylorus and the first part of the duodenum. This was clearly a carcinoma of the stomach because the mucosa of the stomach was involved directly within the pyloric ring. The pyloric muscle was diffusely infiltrated with signet-ring cells and was three times the normal thickness. The tumor had extended grossly for some 2 cm. into the duodenum, which is very unusual; there was considerable infiltration of the surrounding mesentery, and a few of the regional nodes showed microscopic but no gross metastases. There

were no distant metastases from the tumor, the liver and lungs being free. The patient developed terminally a hemorrhagic pleuritis on one side and massive collapse of the left lung. There were no other findings of particular interest.

Dr. Rose's query is the essential question of this case. Why, in a six-week period, despite the use of drugs such as prostigmine and mecholyl, it was never possible to produce a peristaltic wave could not be explained anatomically.

DR. BENEDICT: How much of the mass was outside the stomach?

DR. MALLORY: At the time of autopsy about a third of the tumor lay in the mesentery, but at the time of the first operation no such mesenteric involvement was found.

DR. BREED: Was there any ulcer?

DR. MALLORY: No.

DR. SCHATZKI: Will you describe the gross appearance of the tumor? Was it elevated or infiltrative?

DR. MALLORY: It was entirely infiltrative, consisting merely of thickening of the wall of the stomach and first portion of the duodenum.

DR. SCHATZKI: And the mucosa over it?

DR. MALLORY: Microscopically it was carcinomatous, but it was not ulcerated and was not elevated at any point.

DR. BENEDICT: Did the cancer invade the stomach?

DR. MALLORY: No; that was 15 cm. away.

DR. BENEDICT: You cannot explain why nothing went through the stomach?

DR. MALLORY: No; he had a paralyzed stomach during all this period.

DR. BENEDICT: In this type of obstruction, I do not believe that an anterior gastroenterostomy works as well as a posterior gastroenterostomy.

DR. MALLORY: That was realized but apparently was necessary technically.

DR. MERRILL C. SOSMAN: The small funnel-shaped projection at the lower end of the stomach is probably the infiltrating part of the prepyloric lesion and not an ulcer or projecting tumor.

CASE 29192

PRESENTATION OF CASE

First admission. A forty-two-year-old chemical engineer entered the hospital because of sharp nonradiating pain in the left flank.

The patient had been in good health until three weeks prior to admission, when suddenly, two hours after a sandwich lunch, he experienced a sharp, sticking nonradiating pain in the left flank that lasted five hours and spontaneously cleared. One week later a similar attack occurred, lasted four hours, spontaneously cleared for sev-

eral hours and then recurred for approximately four hours. During this attack he felt slightly nauseated and vomited mucus and partially digested food without relief. There was no change in bowel habits, and no diarrhea, constipation or tarry, bloody or acholic stools.

The family and past histories were noncontributory.

Physical examination revealed a well-developed and well-nourished man who seemed comfortable. The heart and lungs were normal. No tenderness or rigidity of the abdomen was elicited, and no masses were felt. Several small, nontender hemorrhoids were felt just above the anal sphincter. The prostate was small.

The blood pressure was 128 systolic, 82 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 16.4 gm. per 100 cc. and a white-cell count of 7200, with 82 per cent polymorphonuclears. A blood Hinton test was negative. The urine was negative. The stool was brown and guaiac negative. The nonprotein nitrogen was 20 mg. per 100 cc.

A Graham test was negative. There was a laminated area of calcification, about 1 cm. in diameter, in the upper posterior portion of the liver. An intravenous pyelogram was negative. A barium enema filled the colon readily. About 6 cm. proximal to the rectosigmoid junction there was an area of slight narrowing approximately 3.5 cm. in length, associated with gross irregularity of the mucosa with shelf-like margins.

On the tenth hospital day, under general anesthesia, a combined abdominoperineal resection of a carcinoma of the sigmoid was performed and a descending colostomy established in the left paraumbilical region. No tumor was found in the regional lymph nodes attached to the specimen. Very extensive adhesions were present throughout the peritoneal cavity. A number of small nodules, approximately 2 cm. in diameter, were felt but not visualized at the dome of the liver.

Three weeks after operation the patient's temperature began to spike each day between 102 and 103°F. and the pulse showed similar peaks, in spite of a course of sulfadiazine. Two and a half weeks later emetin hydrochloride was administered, and after five days the temperature and pulse became normal. Repeated examinations of the stools did not reveal *Entamoeba histolytica* or its cysts. The patient was discharged eight weeks after admission, apparently quite well.

Final admission (one year later). The patient was readmitted to

that began eight months after discharge from the hospital and became progressively worse.

The patient seemed pale and apathetic and complained of abdominal pain. The colostomy functioned well. The entire epigastrium was distended and tympanitic, and there was tenderness at and below the costal margin in the midclavicular line. Normal peristalsis was audible. No masses were felt. Rectal examination was not remarkable.

The temperature, pulse and respirations were normal.

The blood showed a hemoglobin of 11.6 gm. per 100 cc. and a white-cell count of 6700, with 74 per cent neutrophils. The urine was normal. A bromsulfalein test showed 40 per cent retention of the dye in the serum. The cephalin flocculation test was 0 at 24°C. and + at 48°C. The prothrombin time was 26 seconds (normal, 22 seconds).

A barium meal demonstrated a normal upper esophagus. The lower esophagus showed curling, but in addition, when the esophagus was relaxed, the folds appeared to be widened and tortuous. There was evidence of pressure from the enlarged liver and spleen. The duodenal cap showed similar pressure defects. The remainder of the duodenal loop appeared normal. Hourly films of the small bowel showed rapid passage of the barium. At the end of three hours the barium was in the lower ileum and scattered through the colon to the colostomy opening.

An operation was performed on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EARLE M. CHAPMAN: May we see the x-ray films?

DR. GEORGE W. HOLMES: The obvious finding at the first admission is a large liver. The shadow is of homogeneous density. The diaphragm is displaced upward, and the shadow extends low in the abdomen. In the same region there is a shadow characteristic of a gallstone. On the left side I can see an area of density that is rather characteristic of a large spleen. The examination of the esophagus shows slight prominence of and changes in the mucosal folds, which I am not willing to say are varices, and I take it that whoever examined the patient felt the same way, because he drew no conclusion. I should say that they may be varices, but there is not enough evidence to make a diagnosis.

In the chest films the diaphragm is high on the right, confirming the large liver. The lateral view does not give any additional information.

The plates taken of the gall bladder, strangely enough, show what appears to be a perfectly nor-

mal organ, and the shadow that was thought to be a gallstone is not in the gall-bladder region at all. What it is, I do not know. I do not believe it is a stone in the hepatic duct. Of course that is a possibility, but it is too high.

The film of the stomach is normal. There is nothing in the small bowel. The film of the urinary tract clearly shows the kidney and the injected pelves; they are normal. In the ordinary film the colon does not show anything definite, but the spot films do show the characteristic picture of carcinoma.

To summarize, this patient has a large liver, a large spleen, a shadow in the region of the liver that looks like a gallstone but is not, changes in the esophagus that are insufficient to make a diagnosis of varices, and a definite carcinoma of the colon.

DR. CHAPMAN: The S. S. Van Dyne reconstruction here is a bit difficult. It seems clear that the man had carcinoma of the sigmoid to begin with, and the illness seems perfectly straightforward up to that point. The first warning was an abdominal cramp, and after adequate study they discovered the lesion, which was removed, following which the patient seemed well. Perhaps the clue in this case is the finding of this queer calcified area in the liver. Moreover, there were extensive adhesions throughout the general peritoneal cavity and a number of nodules approximately 2 cm. in diameter that were felt, but not visible, at the dome of the liver. Finally he ran a spiking temperature, which responded to emetin or perhaps, belatedly, to sulfadiazine. If we knew the answer to these various points we could perhaps explain the second illness, which I believe was not related to the carcinoma.

What could cause calcification of this kind? One of course always thinks of tuberculosis as leading to calcification in the course of healing, but tuberculosis of the liver is exceedingly rare. I believe that solitary tuberculomas do occur and they can calcify. One might suppose that some time earlier in life this man had had an infection in his peritoneal cavity that not only left him with adhesions but with nodules and calcification in the liver. The commonest thing I know of which might produce such results is tuberculosis. Other infectious diseases can occasionally heal with calcification but I cannot be specific and name the diseases.

One has to consider the possibility of amebic disease. The patient might have entered with a latent liver abscess that broke down, with subsequent spreading of the disease, but I am against that because the temperature, pulse and respirations were normal on the second admission. One

thinks also of fungus or yeast infection, which may spread through the abdomen and heal with nodule formation.

What are the other possibilities? The first one is carcinoma, metastasizing to the liver and leading to a picture like cirrhosis, with a swollen liver, jaundice, ascites and diarrhea.

This man was forty-two years old and a chemical engineer. That may be a clue. Had he been exposed to some substance that was toxic to the liver? One thinks of carbon tetrachloride, benzene, arsenic and one of the heavy metals. We do not know whether he returned to work.

The presence of straight cirrhosis does not seem likely. The evidence for intrinsic liver damage is not great. It seems likely that the patient had a toxic rather than a cirrhotic liver. The liver, as well as the spleen, was enlarged. The evidence for varices is questionable, as is that for impaired liver function. The flocculation test was 0 at 24°C. and + at 48°C. The prothrombin time was only slightly elevated. His two complaints were diarrhea and fatigue. I should like to know if it is true that he did not have a fever during the second illness. I can hardly believe that, although we are led to believe so with the one statement that the temperature was normal.

DR. TRACY B. MALLORY: The temperature ranged from 97.5 to 100°F.

DR. CHAPMAN: By mouth or rectum?

DR. MALLORY: By mouth.

DR. CHAPMAN: So we cannot accept that statement in the record. The patient did have low-grade fever.

I am curious to know what operation was performed.

DR. MALLORY: It really was not an operation, merely the diagnostic procedure of peritoneoscopy.

DR. CHAPMAN: I should say that this man had a carcinoma of the colon, which was removed. The operation stirred up an old process and he recovered following treatment with emetin hydrochloride, but I do not understand why. There is no evidence for amebic disease. Yet he went on with low-grade fever, diarrhea and weakness and, when readmitted with a swollen abdomen, was obviously ill and going downhill. I cannot believe he had metastatic disease and must assume there was underlying liver disease, possibly a toxic hepatitis connected in some way with his occupation. Finally, some organism that might have caused infection throughout the peritoneal cavity.

DR. MALLORY: Does anyone want to vote in favor of all this being due to metastatic carcinoma? (No response.)

CLINICAL DIAGNOSES

Carcinoma of sigmoid.
 Cirrhosis of liver?
 Amebic hepatitis?

DR. CHAPMAN'S DIAGNOSES

Carcinoma of sigmoid.
 Calcified nodules, abdominal (? cause)
 Toxic cirrhosis (? occupational).
 Peritoneal infection (? cause).

ANATOMICAL DIAGNOSES

Carcinoma of sigmoid, with metastases to re-
 troperitoneal nodes and liver.
 Operative wounds: resection of rectosigmoid
 and colostomy.
 Perforation of bowel, traumatic.
 Peritonitis, acute fibrinopurulent.
 Chiari's disease (thrombophlebitis of hepatic
 veins).
 Splenomegaly with fibrosis, moderate.
 Probable tuberculoma of liver.
 Arteriosclerosis, aortic, severe.

PATHOLOGICAL DISCUSSION

DR. EDWARD B. BENEDICT: At the first attempt at peritoneoscopy I noted a mass of adhesions and could not see anything. I then selected a location a little higher up and found the liver to be full of what appeared to be metastatic carcinoma; this was proved by biopsy.

DR. MALLORY: A decent interval of time after peritoneoscopy, when this man was irrigating the old colostomy, he succeeded in perforating the bowel. He very promptly went into shock and died.

At the time of autopsy we found, as Dr. Benedict had seen, the liver riddled with metastases. These unquestionably came from the original tumor in the sigmoid. However, that did not seem to be the whole story. There was, throughout the second entry, suggestive evidence of portal obstruction. Extremely rarely metastatic carcinoma of the liver does cause portal obstruction. Besides the carcinoma we found that the liver was cirrhotic, a very peculiar type of cirrhosis, which was most marked in the centers of the lobules rather than peripherally, and in a great many of the hepatic veins there was evidence of an old organized thrombophlebitis. I believe it is fair to say that this man had what is known as Chiari's disease,* which is primary thrombophlebitis of the hepatic vein. This would secondarily result in obstruction to the portal circulation similar to that found with cirrhosis of the liver.

The spleen was moderately enlarged, weighing 350 gm. The spleen showed a degree of fibrosis such as one would expect with obstruction of the portal circulation. The folds of the esophageal mucosa were slightly dilated, but no frank varices could be found. The immediate mechanism of death was generalized peritonitis following perforation of the bowel.

DR. HOLMES: Did you find the calcified nodule?

DR. MALLORY: Yes; we made sections of it and are just as wise as we were before. It was a mass of calcium surrounded by fibrous tissue. It lay deep within the liver substance. It could be a healed tubercle; it could be a remnant of a hemangioma, which not infrequently calcifies. There is nothing, however, that gives us any lead to the cause.

*CHIERI H. Erfahrungen über Infarkthildungen in der Leber des Menschen. *Ztschr. f. Heilk.* 19 475 512 1878

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SOCIETY HEADQUARTERS

For several years the Massachusetts Medical Society has discussed the advisability of purchasing a building that, by location and equipment, would constitute a headquarters house. Such a building in a suitable location could undoubtedly be found, but it would require many structural changes, suitable furnishings and a staff of attendants. After the quarters had been created, would the building be used by fellows throughout the State in sufficient numbers to make the project worth while? It is the opinion of the members of the Committee on Society Headquarters and of numerous fellows in and out of Boston that the use of such a house would never justify its high annual

cost. Furthermore, no building would ever meet the full requirements of the Society, especially at the time of the annual meeting.

A considerable number of members believe that the present quarters in the Boston Medical Library give the Society adequate space for the activities of the officers, various committees and the *Journal*, and there is the prospect of additional space in the near future, which will permit the establishment of a medical information center, where visiting physicians may obtain the schedules of meetings and clinics in Greater Boston. The advantages afforded by the books and periodicals of the Boston Medical Library to the staff of the *Journal* are incalculable. Furthermore, the Library can be made increasingly useful to all fellows of the Society, and plans are being formulated with this end in view. In past years the Society has made continually increasing demands on the Library for space, light, heat and service; however, for all these added advantages the Library has never asked an additional penny.

In view of all these facts and opinions, the two recommendations to be presented to the Council at its annual meeting by the Executive Committee—namely, that the Society acquire additional space in the Boston Medical Library and that a greater sum of money be allowed for maintenance—deserve the unqualified support of the members of the Council.

VIRILE NEW YORKERS

THE *New York State Journal of Medicine*,* taking note of an editorial appearing in the March 4 issue of the *Journal*, "Ancient of Days," republishes it in toto, with the following pithy comment:

The begging bowl at sixty may appeal to the senescent New Englander; but, with apologies, we will trail along with Sir William Beveridge. And what have the high Himalayas got, except a little more height, that we lack in the Empire State? We will do our contemplating and service to mankind right here. Our begging bowls were contributed to the scrap drive long ago, and the records of our District Branch meetings showed that attendance in 1942 in the age group 64 to 72 was 15.66 per cent of the total; in the 75 to 84 group, 2.53 per cent; and in the 85

*Editorial. Medicine in the news. *New York State J. Med.* 43:235, 1943.

certain cases; heard on Feb. 16; leave to withdraw on Feb. 18.

- H. 869. Petition of Annie D. Brown that qualified physicians be required to take periodical blood tests and to display certificates of the results thereof in their offices; heard on Feb. 16; leave to withdraw on Feb. 18.
- H. 870. Petition of Annie D. Brown to regulate further the filing of notices of intention of marriage, the delivery of certificates of such intention and the return of unused certificates; heard on Mar. 25.
- H. 871. Petition of Morris Kritzman for the appointment of a special commission (including members of the General Court) to make a survey and study of health needs of certain needy persons within the Commonwealth, heard on Feb. 11; leave to withdraw on Feb. 11.
- H. 1012. Petition of William H. McCarthy (director of the Division of the Blind) for amendment of the law relative to recording the treatment of infants at birth; heard on Feb. 11.
- H. 1013. Petition of William H. McCarthy (director of the Division of the Blind) for amendment of the law relative to reports by physicians of treatment of certain wounds; heard on Feb. 11.
- H. 1014. Petition of G. Lynde Gately (health commissioner of the City of Boston) relative to granting of permits by boards of health to persons engaged in selling, processing, storing and distributing food; heard on Feb. 16; leave to withdraw on Feb. 17.
- H. 1198. Petition of Edwin W. Hadley for legislation to regulate certain experiments with animals; heard on Mar. 25; referred to next General Court Apr. 12.
- H. 1200. Petition of James A. O'Brien that boards of health be required to make monthly inspections of employees of persons distributing food or beverages within their cities or towns; heard on Feb. 16; leave to withdraw on Feb. 17.
- H. 1387. Report of the Commission on Administration and Finance (under authority of Section 7 of Chapter 7 of the General Laws) recommending certain subjects of legislation relative to promoting economy and efficiency and avoiding useless labor and expense within the Commonwealth. So much as relates to permitting the Department of Public Health to establish and maintain cancer clinics; heard on Apr. 8; H. Bill printed in H. 1387, Apr. 12; referred to House W. and M.

COMMITTEE ON INSURANCE

- S. 45. Petition of the Massachusetts Life Underwriters Association, by Merle Summers, for legislation to authorize the issuance of policies of life or endowment insurance without a medical examination and to require the consent of the insured thereto in certain cases; heard on Feb. 7; also on Mar. 29.
- S. 45. Bill to authorize the issue of policies of life or endowment insurance without a medical examination and to require the consent of the insured thereto in certain cases. (Insurance.) In Senate, Mar. 29; ord. 3d, Mar. 30; eng. Mar. 31; rec'd in House, Apr. 1; ord. 3d, Apr. 5; amended and eng. Apr. 6; reconsideration refused, Apr. 7; rec'd in Senate. Senate concurs in amendment, Apr. 8; to Gov. Apr. 13, signed, Apr. 16. Chap. 186.

LEGAL AFFAIRS COMMITTEE

- H. 1141. Petition of Ernest W. Dullea and others for legislation to provide a penalty for theft of domestic animals or birds; heard on Mar. 3; also on Mar. 17; ord. 3d, Mar. 18; H. Bill 1470 substituted, Mar. 30.
- H. 1470. Bill providing a penalty for the unauthorized taking of cats, dogs or birds for certain purposes. Substituted in House, for House 1141, and eng. Mar. 30; rec'd in Senate, Apr. 1; ord. 3d, Apr. 5; amended, eng. April 7; rec'd in House for concurrence in amendment; House concurred, Apr. 8; to Gov. Apr. 13; recalled to Senate, Apr. 20.

A further report, including all the remaining bills to be completed by the legislature, will be published as soon as possible after the closing session of the Great and General Court, the date of which closure will probably be on or about June 1, 1943.

BRAINARD F. CONLEY, *Chairman*

DEATHS

ASH—JOHN H. ASH, M.D., of Quincy, died February 15. He was in his seventy-fourth year.

Dr. Ash received his degree from Harvard Medical School in 1895. He had been a medical examiner for the Metropolitan Life Insurance Company until 1940. He was a member of the Massachusetts Medical Society and the American Medical Association.

A son and six daughters survive him.

DEEMS—OREN M. DEEMS, M.D., of Springfield, died April 17. He was in his sixty-fourth year.

Dr. Deems graduated from the University of Pennsylvania School of Medicine in 1904 and had practiced his specialty—eye, ear, nose and throat in Springfield for many years. He was a member of the Massachusetts Medical Society and the American Medical Association.

DRESSLER—MORRIS L. DRESSLER, M.D., formerly of Cambridge, died May 6 at Fort Dix, New Jersey, where he was serving with the Army Medical Corps. He was in his forty-fifth year.

Major Dressler received his degree from Tufts College Medical School in 1921. He served as Cambridge city physician for ten years and was a trustee of Cambridge City Hospital. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and two sons survive him.

GOLDMAN—HARRY GOLDMAN, M.D., of Roxbury, died April 22. He was in his forty-eighth year.

Dr. Goldman received his degree from Tufts College Medical School in 1918 and held a Master of Public Health degree from Harvard. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, three children and three brothers survive him.

JUDKINS—FRANK L. JUDKINS, M.D., of Lynn, died April 21. He was in his ninety-first year.

Dr. Judkins received his degree from Bowdoin Medical School in 1879 and later studied at Harvard and Dartmouth. A founder of Union Hospital, Lynn, he was the

first president and served for many years as chief surgeon. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and two daughters survive him.

LUTHER—ELIOT H. LUTHER, M.D., of Westfield, died May 2. He was in his forty-eighth year.

Dr. Luther received his degree from Harvard Medical School in 1921. He had been assistant superintendent of Westfield State Sanatorium since 1936 and a member of its medical staff since 1932. He was a member of the Massachusetts Medical Society and the American Medical Association.

PRIEST—HERBERT B. PRIEST, M.D., of Littleton, died March 12. He was in his sixty-ninth year.

Dr. Priest received his degree from the Harvard Medical School in 1901. He was a member of the examining physicians' board of the induction center at Fort Devens and was also a member of the staff of the Community Memorial Hospital in Littleton. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and four brothers survive him.

STONE—THOMAS N. STONE, M.D., of Haverhill, died April 21. He was in his sixty-fourth year.

Dr. Stone received his degree from Harvard Medical School in 1903. He was a member of the Massachusetts Medical Society and of the American Medical Association, and a past president of the Pentucket Medical Association.

WAR ACTIVITIES

CIVILIAN DEFENSE

GAS CLEANSING STATIONS

The following directive (Operations Letter No. 124) has recently been released by the Office of Civilian Defense, Washington, D. C.

(1) In order to avoid confusion in use of the term decontamination, it is recommended that the term be reserved for areas and objects and that hereafter the removal of vesicant liquids from persons be termed 'gas cleansing.' The facilities established for this purpose will be called gas cleansing stations.

(2) The primary purpose of these facilities is the protection of hospitals and casualty stations and their staffs and patients from contamination by injured persons who have been exposed to vesicant agents. Contaminated persons, including Citizens Defense Corps members, who are not disabled, are expected to cleanse themselves in nearby private homes or other local facilities.

(3) In large cities in the target areas, it is recommended that cleansing stations be provided at or adjacent to hospitals in the ratio of one station for 50,000 inhabitants. A station should be provided at every hospital that has 150 beds or more, and if this does not bring the number up to the recommended ratio, additional stations should be established at smaller hospitals or casualty stations. At least one station should be established in every city of 25,000 or more in the target areas.

(4) Under present conditions of scarcity of materials and manpower, construction of new facilities is generally not justified. Cleansing stations should be established in connection with casualty receiving hospitals by conversion of sufficient existing facilities to cleanse persons who are lethally injured and contaminated.

The necessity of using available establishments and materials and avoiding requests for priorities for construction of new facilities cannot be emphasized too greatly. Materials such as pipe, fittings and shower heads must be obtained in the community from available stocks and from suppliers of used and reclaimed equipment.

(5) The chief of Emergency Medical Service and the senior gas officer should assist hospital superintendents in planning their cleansing facilities. In hospitals the facilities which should prove suitable for conversion to cleansing stations, roughly in the order of preference, are hydrotherapy rooms, nurses or interns' locker and shower rooms, part of the outpatient department and garages, or other separate structures. In the event that these are not available, facilities must be arranged in nearby schools, gymnasiums, swimming pools, shower rooms, club houses, and community centers.

Plans should be fully made for immediate establishment and equipment of necessary gas cleansing stations in event of need. It is desirable that each large community establish without delay at least one gas cleansing station for training purposes.

(6) Cleansing stations should be equipped to take care of one third to one half of the hourly casualty receiving capacity of the hospital to be served. The professional staff will consist of mobile medical teams as signed when the station is activated, supplemented by an additional staff of attendants to assist in undressing the injured, moving stretchers, caring for clothing and valuables, maintaining supplies and dressing wounds.

(7) The local chief of Emergency Medical Service is responsible for the development of these stations. The senior gas officer of the community should act as his consultant in helping to establish these facilities. Industrial plants working on war contracts that wish to provide cleansing facilities for employees should be given aid and advice by the chief of Emergency Medical Service and the senior gas officer.

CORRESPONDENCE

MEDICAL SUPPLIES FOR RUSSIA

To the Editor: I should like to use the columns of your valuable journal to extend the thanks of the Massachusetts Committee of Russian War Relief, Incorporated, to the physicians of Greater Boston who have contributed surgical and dental instruments and drugs for transmission to the Russian people. The amount of this contribution has been very large, and literally hundreds of physicians have contributed either instruments or very valuable time for this worthy cause.

Though it is possible that the supply of instruments has now been exhausted, we should be very grateful for any further such contributions. I believe that many physicians will continue to receive medical samples of drugs which would be valuable. We should be most grateful if they would send these to our office at 128 Newbury Street, Boston.

Let me close by again expressing our deep appreciation of the energy and generosity of the physicians of Greater Boston.

HUGH CAPOT, M.D., Chairman
Massachusetts Committee of Russian War Relief, Incorporated

128 Newbury Street
Boston

BOOK REVIEWS

The Eye Manifestations of Internal Diseases. By I. S. Tassman, M.D. 8°, cloth, 542 pp., with 201 illustrations. St. Louis: The C. V. Mosby Company, 1942. \$9.50.

The first half of the book is given to a discussion of the anatomy of the eye, methods of examination of the visual mechanism, and congenital and hereditary ocular anomalies. The second half of the book in page count, but not so designated by the author, treats of the eye manifestations of internal diseases. The text is attractively printed, and its subject matter is enhanced by a wealth of well-chosen, instructive and well-reproduced illustrations, of which nineteen are in color.

In the pages assigned to medical ophthalmology, the author devotes 136 pages to body diseases caused by invading organisms, viruses and parasites, and 133 pages to intoxications, cardiovascular disease, endocrine disorders, avitaminoses, disease and tumors of the central nervous system, skin diseases and disorders of the bones of the skull. In the interest of order, the author gives a brief but significant résumé of each disease, and then recites the ocular manifestations and their treatment. He quotes freely from authorities who have contributed advances during the past decade.

Such an excellent work is a useful "tool" not only for ophthalmologists in teaching and practice, but also for reference by all who practice medicine, make diagnoses and follow the clinical course of disease. In any case, the ophthalmologists do not require, and others cannot quickly assimilate book instruction in the anatomy and methods of examination of the eye. In the opinion of the reviewer, the author might well have cited references to the standard texts that cover these aspects, and then concentrated his whole effort on the wealth of his material in medical ophthalmology, possibly adding more statistical data relating to the incidence of ocular complications, and possibly one chapter dealing with each important eye complication (for example, keratitis, iritis and retinitis) in terms of all bodily diseases that accompany it.

Motivation and Visual Factors. By Irving E. Bender, A.M., Ph.D., Henry A. Imus, A.M., John W. M. Rothney, Ed.M., Ed.D., Camilla Kemple and Mary R. England. 8°, cloth, 369 pp. Hanover, New Hampshire: Dartmouth College Publications, 1942. \$4.00.

One quarter of the Class of 1940 at Dartmouth College, during their four years of college life, became willing subjects to detailed eye studies by the staff of the Eye Institute, to periodic medical and neurologic examinations by the Health Service and to autobiographies dealing with their familial socioeconomic background, and during the fourth college year one sixth of these students submitted to repeated interviews by the authors of this monograph. To probe the relation between motivation and visual abnormalities, the authors constructed 20 complete case histories, which are reported in detail in the fifth chapter of the monograph, and which reflect for each subject the four-year eye findings, the adaptation to the college community, the scholastic achievement, the observed personality and behavior of the subject, and his intelligence and performance as determined by standard tests.

The interest of these studies to psychologists will center around the psychologic approach by interview and questionnaire, the methods selected for the subjective and objective appraisal of each patient, and the validity of analysis and interpretation by the authors of the 20 psychoportraits, each of which seeks to portray fully the manner in which the individual copes with and adjusts himself to his environment. For the thoroughness of methods and the frankness of interpretation of the findings one can have only admiration. But in view of the conflicts and frustrations that beset everyone daily from birth onward, and with respect to the conditioning that one who survives must acquire in thousands of contacts with a hostile world, one must rate the question of validity of interpretation based on the span of a few years, the isolated college years.

The interest of this monograph to physicians, and especially to ophthalmologists, will focus on the six general conclusions which the authors voice in the sixth chapter. In substance, admitting that the visual abnormalities demonstrated were mild, the authors deny any significant effect on motivation by the corrected or uncorrected visual abnormalities (oculomotor anomalies, refractive errors, aniseikonia and so forth); they deny a demonstrable relation between visual efficiency and academic grades and tested mental ability; and they deny that provision in college of indicated optical corrections yielded improvement in the quality of scholastic achievement. There is speculation about the effect that might be precipitated deliberately by an artificial aniseikonia in a patient previously normal, and therefore in one who has had no occasion or opportunity to condition himself to such a problem.

As in all discerning research, the work at Dartmouth has opened up new problems, and the high quality of investigation there promises answers to them.

Treatment in General Practice. By Harry Beckman, M.D. Fourth edition, thoroughly revised. 4°, cloth, 1015 pp., with 20 tables, 1 chart and 5 illustrations. Philadelphia: W. B. Saunders Company, 1942. \$10.00.

This is the fourth edition of a book that has been favorably received by the profession since its original publication.

The author has justifiably deplored the situation prevalent in medical schools limiting therapeutics to a course in pharmacology and then ignoring formal teaching in the treatment of the sick patient. Without belying the importance of diagnosis and the search for specific remedies, the relief sought by the patient can be abetted in countless ways. The book amply satisfies these needs and can be utilized alongside a text of medicine. For the man in practice it offers a source of quick reference easily appreciated.

The author has refrained from delving into questions of specialized treatment or technic. The integration of clinical medicine and physiology has borne fruitful results in a rational approach to therapy. One omission worth noting is a discussion of the treatment of intestinal obstruction, which in its presurgical phases, involving the restoration of the chemical equilibrium of the body, has been of life-saving value.

One cannot help remarking on the smooth style of the writing itself.

(Notices on page xi)

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SPINA BIFIDA AND CRANIUM BIFIDUM*

II. Surgical Treatment

FRANC D. INGRAHAM, M.D.,† AND HANNIBAL HAMLIN, M.D.‡

BOSTON

THE treatment of myelomeningocele and encephalocele constitutes one of the major problems of pediatric neurosurgery. The lesion may occur at any point of the dorsal axis, usually but not invariably associated with bifid vertebral anomalies or defects in the skull. These protrusions exhibit great diversity in appearance and histologic components. The distribution, frequency of various types and so forth have been tabulated in a previous communication¹ and the clinical features have been repeatedly described.

Pathologically, myelomeningocele is regarded as representing the result of incomplete and abnormal dorsal fusion that takes place relatively early in embryologic life. The defect or defects thereby produced involve structures inherent to and surrounding the central canal and its contents in variable degree at one or several segments, which may be conjoined or separated by normal intervening anatomical units.

The selection of patients who are likely to be amenable to long-range rehabilitation and the choice of the proper time for operation are of paramount consideration before the question of surgical procedure arises. In some cases the membrane may be so thin and fragile that operation must be carried out immediately to avoid rupture and subsequent meningitis. Occasionally we have removed such protrusions the first day of life, in spite of the fact that it was impossible to give an adequate prognosis at such an early age. Usually, however, there is no need for haste and careful evaluation of the infant, including roentgenologic examination, should be made. The size of the lesion and the nature of its protective coverings are noted. Many of the more formidable

ones have a central sac or loculation that is covered externally by a relatively large area of delicate membrane, and one is obliged to await peripheral epithelialization to obtain sufficient tissue for closure, even though the skin eventually available may be cicatrized, uneven and of poor tensile strength.

There may be additional scoliosis, vertebral fusion, absence of ribs or other skeletal abnormalities. Predominating in lumbosacral lesions, talipes equinovarus or valgus is often present and is likely to be accompanied by faulty innervation of the sphincters and lower limbs. Inept control of the latter may not be apparent for weeks or months. Clubfoot deformity and paralysis presage a long course of orthopedic treatment, which can be instituted immediately but often cannot be satisfactorily continued until the tumefaction of the lower back is reduced and given adequate skin protection. These factors combine to produce confusion and indicate that temporization with home care and out-patient visits forms the proper basis of treatment until the infant can be fairly appraised with respect to future promise. There are patients with open marsupialization of the lesion who will not survive long. Other handicaps, particularly poor mental endowment, render surgical success highly improbable. On the other hand, certain patients in whom the outlook seems to be almost hopeless during the early months of life will in time progress to a point where surgery is both feasible and advisable. For example, an infant is examined at a few weeks of age and is found to have a myelomeningocele surrounded by barely enough skin for closure; there are also clubfoot deformity, marked neurologic disorders and hydrocephalus. At the age of two the hydrocephalus has stabilized and the child shows adequate sphincter control and a chronological mental status. Epithelialization of the lesion has great-

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†Neurosurgeon, Children's Hospital, associate in neurosurgery, Peter Bent Brigham Hospital; assistant in surgery, Harvard Medical School.

‡Fellow in neurosurgery, Children's Hospital, and assistant in surgery, Harvard Medical School.

ly reduced the operative risk; after successful repair the residual physical disability can receive full benefit of orthopedic surgery. One must be very slow to give a definite prognosis in such cases, even in the severe grades of the deformity.

Among the congenital anomalies associated with myelomeningocele, hydrocephalus offers the greatest difficulty from the standpoint of selection of cases for surgery and their prognosis. The abnormality may be recognizable at birth with palpable diastasis of fontanelles and cranial sutures and craniolacunia (*Lükenschädel*) present roentgenographically. Conservative home care is obviously to be recommended as the initial phase of treatment in such cases. Sometimes, however, the disturbance is insidious, enlargement of the head becoming apparent shortly after the myelomeningocele has been well repaired. Repetition of this sequence of events is probably responsible for the myth that removal of a meningocele and its spinal fluid reservoir is liable to cause an ensuing hydrocephalus. Delay in surgical intervention, therefore, is the wisest general course to pursue even in some of the simpler forms of the syndrome. The small meningoceles, especially the cervicodorsal protrusions, in infants who are neurologically normal and show no roentgen defect other than a localized spina bifida can be operated on during the first days or weeks of life with a good outlook. The complicated cases, however, in which the myelomeningocele usually is lumbosacral, compel a decision to wait until accurate appraisal of the problem can be formulated during the early period of rapid growth and development. Thus, the best surgical procedure for the given situation and its aftermath, which may be the most perplexing part of the treatment, is carried out with confidence.

The most important feature of the actual operation is the adaptation of whatever technic is used to the case in hand. The elaborate approach necessary to deal safely with nasopharyngeal protrusions will be described in a later communication. The specialized treatment of orbital protrusions has been described by Dandy.² Anterior protrusions into the thoracic and abdominal cavities should not be difficult to deal with if a meticulous closure of dura is made and is reinforced by bringing stronger adjacent tissues together over the closure. The disastrous result of failing to make a secure dural closure is illustrated by the following case history.

CASE 1 (C. H. 168203). A 5-month-old male infant was transferred to the Surgical Service on February 14, 1933, for treatment of a retrorectal tumor. The patient had been admitted with a history of dysuria and oliguria of 16 days' duration. During this time there had been progressive distention of the abdomen and increasing

constipation. Catheterization had been necessary at frequent intervals.

Physical examination showed a well-developed and well-nourished infant in no apparent distress. A soft, smooth, rounded mass the size of a small orange was



FIGURE 1. Barium Enema Showing Marked Displacement of the Large Bowel by a Pelvic Anterior Meningocele.

palpable by rectal examination about 6 cm. above the anal sphincter. X-ray examination showed marked distortion of the large-bowel shadow by the pelvic mass (Fig. 1). Two days later, abdominal exploration was carried out and the cystic mass found to fill the entire pelvis. It was separated from the surrounding structures down to the sacrum, where it was found to be densely adherent. At this point the cyst was aspirated and clear, faintly yellow fluid was removed. It was thought that total removal was impossible, and a portion of the wall was excised, permitting the fluid to drain into the peritoneal cavity. Following operation there were severe vomiting and diarrhea, which gradually subsided. As the general condition improved rectal examination showed that the cyst had reformed. Nineteen days after the first exploration a secondary operation was done and the sac was sutured to the peritoneum. The patient's condition was extremely poor at the end of this procedure and he died 28 hours later.

Permission for autopsy was not obtained, but sections of the cyst wall showed it to be undoubtedly the wall of a myelomeningocele containing typical dura and a small, irregular mass of glial tissue.

In retrospect it seems relatively certain that the vital step in the operative procedure in this case—that is, firm closure of the sac—was entirely omitted. Total removal of the sac was apparently impossible but was also unnecessary, and firm closure

sal, lumbar and lumbosacral (Figs. 4, 5, 6 and 7)—are tight closure of the sac and firm closure of the skin and subcutaneous tissue. Reinforcement of the closure with fascial leaves is desirable if this can be done without prolonging the operation



FIGURE 2. *Simple Cranial Meningocele with Only a Small Stalk Extending within the Cranial Cavity.*

of the remaining portion, with the formation of a small secondary meningocele, would probably have given a satisfactory result.

Protrusions through the cranial vault are relatively simple to deal with. The bony defect is not unusually large, and firm closure of the dura and galea, with the incision adapted to the size and shape of the defect, are all that is necessary (Fig. 2). Low occipital encephaloceles are likely to present a much more complicated problem. These masses are sometimes extremely large, and the decision whether or not operation should be done may be difficult. If marked abnormality of the brain or poor function below the lesion is demonstrable, operation should not be considered. Occasionally one sees an extremely large occipital meningocele or encephalocele that gives the impression of a hopeless outlook when the brain is actually normal (Fig. 3). It is advisable to postpone any estimate of the prognosis until a complete study has been carried out.

The two essential features of any operation on the commoner protrusions—that is, cervical, dor-

sal, lumbar and lumbosacral (Figs. 4, 5, 6 and 7)—are tight closure of the sac and firm closure of the skin and subcutaneous tissue. Reinforcement of the closure with fascial leaves is desirable if this can be done without prolonging the operation unduly. Reconstruction of the bony canal should never be attempted at this time, but if the defect is such that the bony spine is seriously weakened, a secondary procedure with a bone graft may be done. If the patient is given proper orthopedic care, this should seldom be necessary. In the typical case an elliptical incision (Figs. 8 and 9) is made around the base of the mass, preferably preserving enough healthy skin to be brought together without tension. If this is impossible and operation cannot be postponed until there is enough skin, counterincisions may be made or a Z flap of skin brought over the defect. In the case of lumbar and lumbosacral lesions, the incision should always be made transversely so as to keep the wound as far as possible from the intergluteal fold.

Dissection is carried down to the neck of the sac, carefully avoiding any nerve elements that may be running out from the sac. The sac is then opened through an area, preferably midline, that can be shown to be free from nerve tissue. The interior of the cavity is inspected, nerve tissue

ending in the wall is sacrificed, and nerves that may possibly be functioning are carefully preserved. The major portion of the sac is then cut away, leaving sufficient tissue to overlap the edges enough to make a secure closure. If there is a

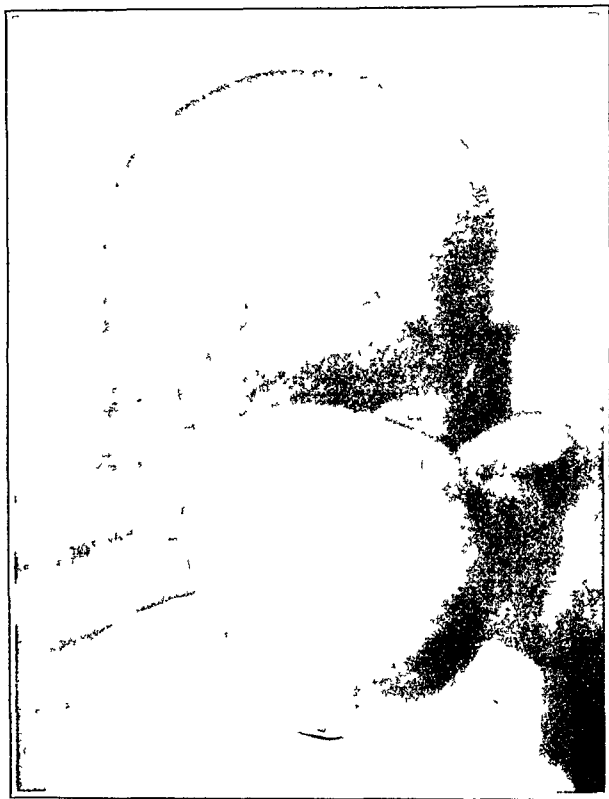


FIGURE 3. *Large Occipitocervical Encephalomeningocele Removed at the Age of Two Weeks.*

large amount of tissue that may have potential function, it may be necessary to create a small secondary meningocele to preserve it. In our experience, plication of the sac, as advocated by Penfield,³ has had no bearing on the development of hydrocephalus postoperatively. In fact, the meningoceles with sufficient skin to make plication of the sac possible are those milder grades of maldevelopment in which one would not expect hydrocephalus to be present.

The first postoperative week is an extremely critical period because of the danger of spinal-fluid leakage, infection at the closure site and possibly meningitis. The hazard increases with the size and complexity of the lesion. If there is any doubt about the possibility of making a firm closure, prophylactic administration of a sulfonamide, preferably sulfadiazine, is recommended starting forty-eight hours prior to anesthesia and maintaining an effective blood level for at least one week. Ideal aftercare consists of proper initial and subsequent dressing of the wound and the use of specialized methods for regulating cerebrospinal-

fluid pressure. Diligent nursing is essential. Complications, if they arise, should be recognized and treated quickly. The particular problems in the postoperative care of the lumbar and lumbosacral types of protrusion are discussed in some detail below.

Before the wound itself is dressed following operation, an apron of sheet rubber or strong oiled silk is glued across the buttocks below the surgical field to protect this area from contamination by excreta.

A routine dressing of sterile sponges over silver foil covering the skin is satisfactory for the small, well-approximated incision, which is the result in many lesions. Anxiety about delayed healing and spinal-fluid leakage is more likely to be felt in the lumbosacral type. When good approximation is achieved following the evacuation and obliteration by suture of a large subcutaneous meningocele, the skin flaps, despite exact alignment, are sometimes loose. In this situation, dead space between the fascial planes can be minimized during the important stage of primary union by taping a small sandbag on the dressing and leaving it there for twenty-four to forty-eight hours. The pad of sponges should be fastened to the skin with adhesive strips running at right angles to one another, leaving interstices of gauze exposed for circulation of air.

In addition to meticulous dressing, conscientious nursing in the supervision of a few specialized techniques, adapted to the aftercare of these patients, contributes toward shortening their immobilization, which is usually prolonged under the best conditions. Figure 10 shows the basic setup used postoperatively at the Children's Hospital for cases of myelomeningocele. A Bradford frame is supported by blocks front and back on the mattress of an ordinary crib bed with side drops. The usual rubber sheet crosses the midportion of the mattress, upon which a bedpan rests beneath an overlying aperture in the canvas. A half-cylinder frame keeps the bedclothes away from the surgical area. A clean diaper is kept under the protective apron, which is sealed off above the buttocks. Diapers are applied in the usual fashion when there is no risk of contaminating the dressing or when healing is well advanced. Fitted on the supportive swaths of the Bradford frame are mattress covers over which are stretched and taped layers of Pliofilm or cellophane, which afford excellent protection to infant skin. The patient lies prone as illustrated, and is so maintained by cloth binders around the trunk and upper thighs and a combination of wrist, shoulder and ankle restraints, well padded with sheet wadding. The restraints are varied accord-

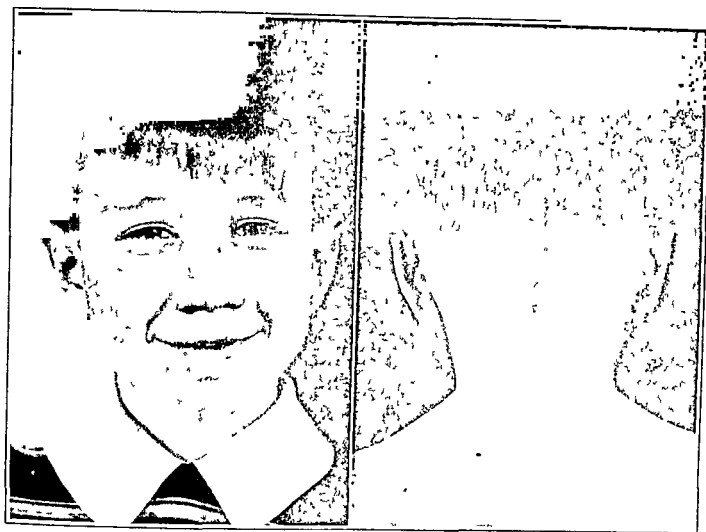


FIGURE 4 Same Patient as in Figure 3 Seven and a Half Years after Operation

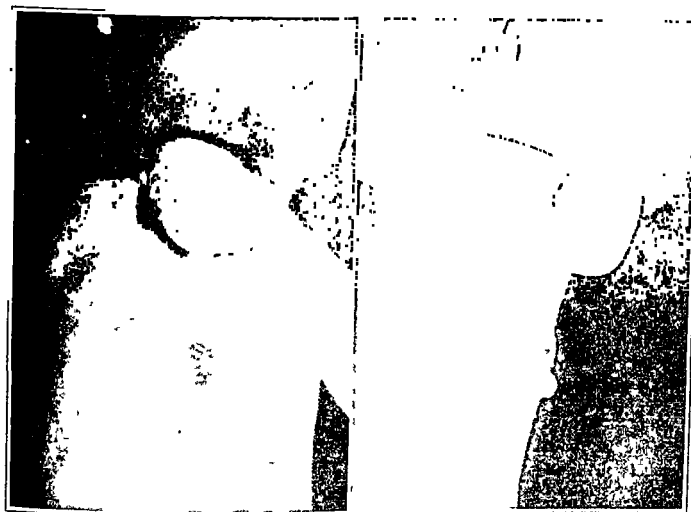


FIGURE 5 Combined Cervicodorsal and Lower Dorsal Myelomeningocele without Impairment of Function



FIGURE 6. *Preoperative and Postoperative Photographs of a Sixteen-Day-Old Infant with a Large Dorsal Myelomeningocele.*



FIGURE 7. *Large Myelomeningocele Involving the Lower Dorsal and All Lumbar and Sacral Segments.*

The patient had an arrested hydrocephalus, and paralysis of the lower extremities and sphincters. The case was not suitable for operation.

ing to the horizontal plane of the frame but with constant regard for maximum comfort. Feeding, bathing and other nursing details are easily ac-

If there is undue tension or other reason for examining the wound at frequent intervals, a transparent dressing can be easily prepared (Fig

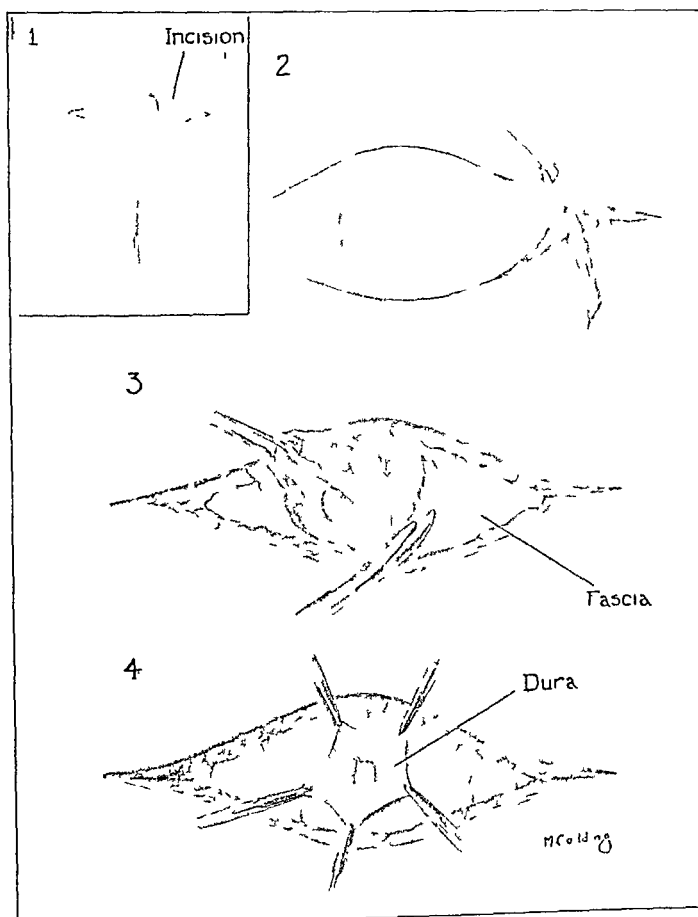


FIGURE 8 Type of Incision and Dissection Used for Most Lumbar and Lumbosacral Protrusions

complished, since the whole frame can be picked up and moved whenever necessary without disturbing the patient. As convalescence progresses the child is allowed gradual freedom of posture by altering the restraints until he is completely mobilized.

11) By this means the operative field can be inspected without removing the dressing and given immediate care should the need arise. Overtight sutures are removed before necrosis starts any point of the suture line that appears weak may be sealed by a cutaneous silver clip and an incipi-

ent leak perhaps prevented. If superficial infection develops, it can be checked at the onset. A wall of gauze at least 5 cm. deep is built around the wound by layering sponges folded or trimmed to appropriate size. These are secured to the skin and to one another by means of sterile

ture or ventricular drainage. If all goes well, the window is left for eight to ten days, at the end of which time a conventional dressing can be substituted.

Occasionally, in spite of all precautions, temporarily increased cerebrospinal-fluid pressure be-

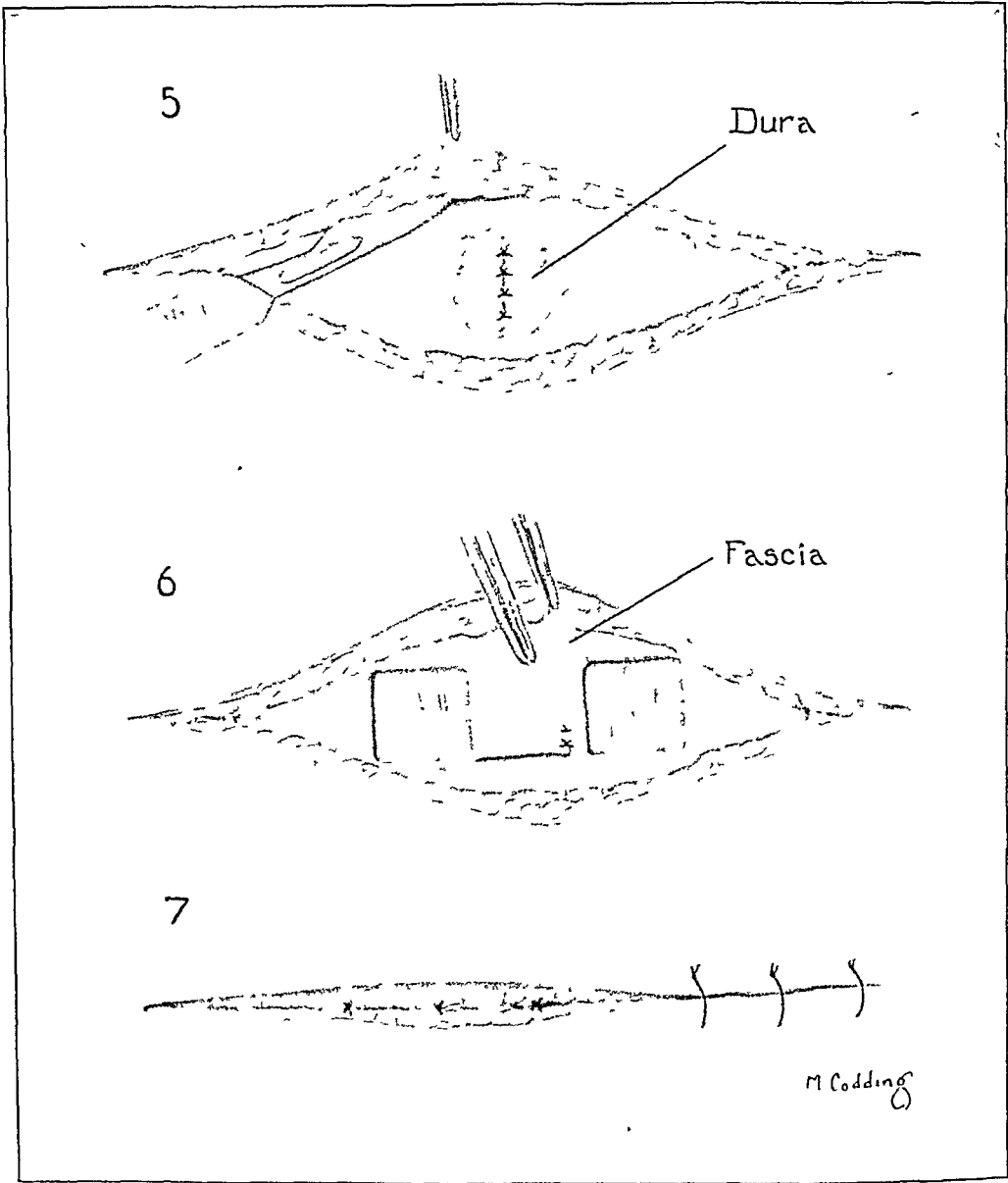


FIGURE 9. Closure Re-enforced by Fascial Flaps.
This step must frequently be omitted.

glue, such as Mastisol. A piece of transparent plastic material is then cut to overlap generously the opening in the dressing. Finally the whole is bound down with adhesive bandage and tape. If spinal-fluid leakage is detected during the critical stage of healing, the development of a fistula is preventable by prompt measures such as applications of warm physiologic saline solution and the reduction of intracranial pressure by lumbar punc-

comes a serious menace. In these cases gravity can be utilized to a certain degree by keeping the head end of the Bradford frame several centimeters lower than the foot with proper-sized blocks. In lumbosacral wounds the head-down position requires that extra vigilance be maintained over excretory cleanliness.

Where the pressure is not controllable by periodic tapping, we have used a simple system of

constant lumbar drainage that has proved effective. A small-gauge (No. 20) needle is thrust

convenient interspace relative to the dressing. When a free flow of spinal fluid is obtained, the

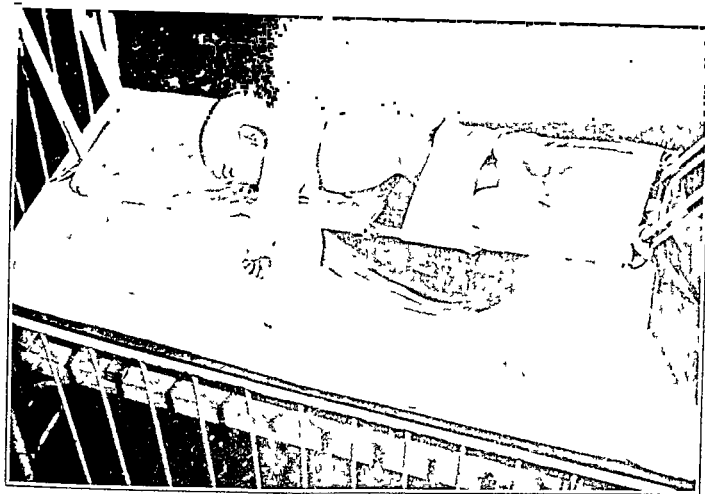


FIGURE 10 Postoperative Dressing and Immobilization of Patient



FIGURE 11 Postoperative Wound Twenty-four Hours after Application of Transparent Dressing.

A sterile cork measuring approximately 3 cm. and is inserted in the caudal sac at a

needle is connected by an adapter to an autoclaved gravity apparatus, as shown in Figure 12. The apparatus consists of narrow rubber tubing, broken at one point by a medicine dropper for inspection of patency and connected to a 25 cc. burette. The needle is held perpendicular by taping the cork to the skin. The burette is suspended on the side gate of the crib so that hydrostatics can be regulated to produce the desired rate of flow by raising or lowering the reservoir as indicated by its fluid meniscus. Daily output is measured, and varies according to the time required for stabilization of cerebrospinal fluid dynamics. An apparatus similar in principle and design was originally described by Ingraham and Campbell⁴ for constant ventricular drainage. It can be kept in continuous operation, however, longer by the spinal route than by the ventricular without the risk of meningeal contamination that goes with the latter. This assumes that the dynamics will ultimately stabilize at a physiologic level, which is usually the case if there has not been progressive hydrocephalus preoperatively. If there has been increasing pressure, operation should not have been carried out.

The following summary of the first case of postoperative myelomeningocele in which this technic was applied demonstrates how constant spinal drainage solved a difficult problem of leakage and fistula.



FIGURE 12 *Control of Cerebrospinal Pressure by Continuous Spinal Drainage*



FIGURE 13 *Lumbosacral Myelomeningocele with Associated Deformity of Lower Extremities.*

CASE 2 (C H 256381). A 2 year old boy was admitted on October 15, 1941, with the complaint of paralysis of the lower extremities and a lump on the back (Fig 13). There was no hydrocephalus and the patient was normally alert and responsive. On the 9th hospital day the meningocle was excised and closure was carried out under tension. Seven days later a cerebrospinal fluid leak developed from the central portion of the incision. Sulfadiazine was started by mouth and an attempt was made to close the leak by resuturing the wound. Three weeks later a third attempt was made and the leak was satisfactorily closed. A lumbar puncture needle was passed into the upper lumbar subarachnoid space according to the technique described above and 200 to 300 cc. of cerebrospinal fluid was drained every 24 hours for 7 days. At the end of this time the wound was firmly healed. There have been no further complications. It seems reasonable to assume that, without the continuous drainage above the site of the incision, healing would not have occurred and infection would finally have developed.

SUMMARY

The essential features of the satisfactory treatment of congenital cranial and spinal protrusions are the selection of patients suitable for operation, simple removal and repair of the defect adapted to the location, size, and shape of the protrusion and meticulous postoperative care. It should be emphasized that a definitely hopeless prognosis should very rarely be given at the first examination.

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ISOIMMUNIZATION WITH Rh FACTOR IN ACQUIRED HEMOLYTIC ANEMIA*

Report of a Case

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THE following case of acquired hemolytic anemia is reported because of several unusual features, among which was the development of an anti-Rh agglutinin with subsequent violent transfusion reactions. The presence of immune hemolysins in cases of acquired hemolytic anemia has been noted by Dameshek and Schwartz¹⁻³ in previous communications. These observers produced hemolytic anemias of varying degrees of severity in guinea pigs by the injection of a hetero-hemolytic serum.² Although many cases of acute hemolytic anemia, with and without hemolysins, are cured by splenectomy, others fail to respond. The opinion was expressed by Dameshek and Schwartz³ that the continued hemolysis in some cases might be due to the development of isoimmunization as the result of repeated transfusions of blood. In the present case, successive transfusions finally resulted in the development of extreme and almost fatal hemolytic reactions. Subsequent analysis of the patient's and donors' blood revealed that the patient (Group O, Rh-) had become immunized by Rh agglutininogen as evidenced by the presence in the patient's serum of

anti-Rh agglutinins. Splenectomy revealed intense myeloid metaplasia, and biopsy of the liver showed an extreme erythroblastic reaction, suggesting the histologic picture of erythroblastosis foetalis. Shortly after splenectomy, the patient died of acute (toxic) necrosis of the liver.

CASE REPORT

L. P., a 49 year old housewife, was admitted to the Joseph H Pratt Diagnostic Hospital on November 20, 1941. The family and past histories were irrelevant. She had given birth to one child without incident 18 years previously. In 1938, because of a sore throat she was given sulfanilamide. A toxic rash shortly developed. Since this illness, the patient had complained of fatigue and weakness, and had seen her physician on numerous occasions. However, she managed to continue her regular duties until July, 1941, when during a visit to the mountains, she complained of a throbbing headache, and developed vomiting and diarrhea. On returning home, she consulted her physician, who found that she was anemic and prescribed iron and liver extract. No response occurring, she was admitted to the Mercer Hospital (Trenton New Jersey) on August 28, 1941, where she was found to have a hemoglobin level of 29 per cent and a red cell count of 1,460,000. Transfusions of compatible blood (Group O) were given on August 28, 29 and 30 without incident. On September 2, the hemoglobin was 52 per cent and the red cell count 2,770,000. Despite this improvement, three transfusions, each of 300 cc., were given on September 4, 5 and 6 from the same donors, again without reaction. On September 13, the hemoglobin was 51 per cent, and the red cell count, 2,630,000. Four transfusions were again given on

*For the Joseph H Pratt Diagnostic Hospital and the Blood Laboratory, Boston, Massachusetts, and the Division of Laboratories, Newark Beth Israel Hospital, Newark, New Jersey. Aided by a grant from the Clurman Fund, Tufts College Medical School.

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Group O donors whose bloods were compatible by the slide cross-matching technic. Severe transfusion reactions began with the September 18 transfusion (the eighth). This transfusion and those on the 19th and 20th were followed by violent reactions characterized by high fever, marked jaundice and tenderness in the splenic region.

The patient's condition became rapidly more critical. On September 23, the hemoglobin had dropped to 34 per cent and the red-cell count to 1,700,000. Another transfusion was ventured on September 27, and was fortunately without reaction. However, the patient's condition continued precarious, with increasing anemia, jaundice and fever. On October 1, normoblasts were first noted in the blood smear. On October 4, a consultant thought that "a hemolytic anemia would seem to best fit the picture" and suggested continuance of liver extract and the avoidance of further transfusions. He stated his belief that splenectomy was too great a risk to be undertaken. Fol-

siderin was present. The blood bilirubin gave both direct and indirect reactions and varied between 3.1 and 4.0 mg. per 100 cc. The fecal urobilinogen content was 716 mg. daily (average of 4-day sample), and the hemolytic index⁴ was thus approximately fifteen times normal. The blood prothrombin was 35 to 40 seconds (normal control, 25 to 30 seconds). X-ray films of the chest showed a slight increase in the lung markings and marked dilatation of the heart, which was thought to be due to the anemia.

The patient's blood was Group O and Rh-. The serum contained no autoagglutinins or iso-hemolysins, but preliminary tests showed the presence of a strong atypical isoantibody that agglutinated the red cells of 19 of 34 Group O individuals. It was suspected that this isoagglutinin might correspond to the anti-Rh agglutinin, and in most cases tested there was a direct correlation between the reaction of this serum and those of two known human anti-Rh testing serums. However, because of the several

TABLE 1. Summary of Data on Transfusions.

NO OF TRANS-FUSION	DATE	NAME OF DONOR	AMOUNT OF BLOOD GIVEN cc.	DONOR'S BLOOD GROUP	PATIENT'S RHD-CELL COUNT $\times 10^3$	REACTION TO TRANSFUSION
1	8/28	W. H. P.	500	O, Rh-	1.46	None
2	8/29	R. P.	500	O, Rh-		None
3	8/30	J.	500	O, Rh+		None
4	9/4	W. H. P.	300	O, Rh-	2.77	None
5	9/5	R. P.	300	O, Rh-		None
6	9/6	J.	300	O, Rh+		None
7	9/17	Je.	500	O, Rh-	2.63	None
8	9/18	M.	500	O, Rh+		Moderate
9	9/19	R.	500	O, Rh+		Increasing jaundice
10	9/20	D.	500	O, Rh+		Extreme, with chill and marked jaundice
11	9/27	F.	500	O, Rh-	1.70	None
12	10/4	R.	250	O, Rh+	.80	Severe abdominal pain, hemoglobinuria, jaundice, confusion and so forth
13	11/25		500	O, Rh-	1.50	None
14	11/28		500	O, Rh-	1.75	None
15	11/30		500	O, Rh-	1.70	None
16	12/1		500	O, Rh-		None (splenectomy)
17	12/3		500	O, Rh-	1.86	None
18-19	12/5		1000	O, Rh-	2.08	None

lowing a transfusion of 250 cc. on October 24, the patient became semiconscious, greatly jaundiced and confused; the hemoglobin dropped to 15 per cent and the red-cell count to 800,000. Injections of hypertonic glucose given intravenously were followed by gradual improvement and a rise in the blood levels on November 12 to a hemoglobin of 36 per cent and a red-cell count of 1,800,000.

On November 19, when first seen by one of us (W.D.), the patient was extremely pale and moderately icteric. The heart appeared slightly enlarged, and a systolic murmur was present. The liver edge was readily felt three fingerbreadths below the right costal margin and a rounded, firm splenic edge extended a handbreadth below the left costal margin. The clinical diagnosis of acquired hemolytic anemia was made and the patient was transferred to the Pratt Diagnostic Hospital for further study and treatment.

On admission, the patient showed hemoglobin values of 3.6 to 3.8 gm. (23 to 24 per cent), red-cell counts of 1,390,000 to 1,650,000, platelets 775,000, reticulocytes 22.5 to 49.3 per cent, and a white-cell count of 8150, with 53 per cent mature neutrophils, 14 per cent immature neutrophils, 27 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. The hypotonic sodium chloride fragility was 0.48 to 0.20 per cent and the acid fragility (Ham) test negative. The urine showed small amounts of bilirubin and 2.8 mg. of urobilinogen excretion per day (normal 1 to 3 mg.). There was no urinary hemoglobin (benzidine test), but a small amount of hemo-

discrepancies noted, further immunologic tests were performed in the laboratories of the Newark Beth Israel Hospital. These tests showed two types of agglutinins, a variety of the anti-Rh warm agglutinin, now called anti-Rh₂, and a cold agglutinin. These are discussed below.

It was thought that the patient had become isoimmunized against the Rh agglutinin as the result of the numerous transfusions that had been given. Through the co-operation of the patient's husband and the Mercer Hospital, blood was obtained from all the donors previously used, and these samples were tested for the Rh factor. The results are shown in Table 1 and indicate the likelihood of isoimmunization by Rh+ blood, the patient herself being Rh-. The patient's family represented an example of the rare double Rh- mating, both the husband and the son being Rh-. The transfusions of donor J. (Rh+), given on August 30 and September 6, were apparently sufficient to induce isoimmunization, since the administration of Rh+ transfusions on September 18, 19 and 20 were followed by violent hemolytic reactions. When another Rh+ transfusion was given on October 4, death almost occurred.

In Boston, Group O compatible Rh- donors were obtained, and transfusions of 500 cc. were given on November 25 and 28, without incident. The patient was then transferred to the care of Dr. Leland S. McKittrick at the Palmer Memorial Hospital, where splenectomy was performed under Avertin and cyclopropane anesthesia on December 1. The postoperative course was at first satis-

factory, but the patient then became rapidly more icteric and drowsy. The red cell count dropped precipitously, — from 1,600,000 on December 3 to 800,000 on December 4 — and the reticulocyte percentage fell from 31.5 per cent on December 2 to 1.9 per cent on December 8. Despite several transfusions from Rh- donors, intravenous fluids and so forth, the patient's condition rapidly became worse. On December 8 the bilirubin value was 25.9 mg. per 100 cc and the red cell count was 740,000. The patient died on December 9 in coma.

The spleen, which weighed 750 gm., showed hemosiderosis and myeloid metaplasia with large islands of erythroblastic cells and rather few leukocytic cells. Two necrotic areas, probably due to previous infarctions, were also present. Hemolysis of red cells, both within and without the sinusoids, together with agglutinated masses of red cells was seen. A section of liver removed by biopsy at the time of splenectomy also showed myeloid metaplasia with erythroblastosis predominating. The histologic appearance of the liver was strikingly similar to that seen in erythroblastosis foetalis.

Autopsy. Sections of the liver showed extensive necrosis, the appearance being greatly different from that of the biopsy specimen (the acute necrosis may have been related to the Avertin given as a primary anesthetic agent prior to splenectomy). Evidences of myeloid metaplasia were present in the kidney, adrenal glands, lymph nodes and so forth.*

COMMENT

This case illustrates the development of isoimmunization following repeated transfusions. The recent investigations of Landsteiner and Wiener⁷ and of Levine et al.¹⁰ have demonstrated the presence in human red blood cells of an Rh agglutinin, its inheritance as a Mendelian dominant and its ability to cause isoimmunization. Two different methods of isoimmunization are possible: isoimmunization of an Rh- recipient by repeated transfusions with Rh+ blood¹¹ and isoimmunization of an Rh- mother by Rh+ red cells from the fetus in utero via the placenta.⁷ The data in this case demonstrate the former. As a result of this isoimmunization, an Rh- woman during pregnancy, having built up an anti Rh agglutinin, might conceivably suffer from an intragroup hemolytic reaction if transfused with blood from an Rh+ donor, or her serum might react in utero with the fetus's red cells, causing erythroblastosis foetalis. That these contentions are correct has been abundantly shown.⁹ Although exact data on the development of isoimmunization of an Rh- recipient through the administration of Rh+ blood are usually lacking, it was possible in the present case to gather data that leave little doubt of isoimmunization by the subsequent development of an anti Rh agglutinin (Table 1).

The presence of two types of atypical agglutinins is demonstrated in Table 2, in which are recorded the parallel results of three series of tests of the patient's serum with eight selected

TABLE 2 Tests with Serum of Patient at Various Temperatures and with Known Human Anti Rh Serums

Cells of Cx. P. O. Subjects	F 51	B*	S	I	C	S	III	KNO. ANTI RH SERUM	HUMAN SERUM
								1†	2‡
1		0					+	+	+
2							+	+	+
3							+	+	+
4							+	+	+
5		0					+	0	+
		(+	0	+
							+	0	+
8							+	0	0

Tests at 10°C and 15°C in human serum for one and a half hours.
 Tests at 10°C and 15°C in human serum for one and a half hours.
 Tests at 37°C in serum reactions with random human red cells.
 Tests at 37°C in serum reactions with random human red cells.

Group O cell suspensions, at 37°C (IA), at 20°C (II C), and at icebox temperature (III). The readings were all made after one and a half hours' incubation at the stated temperatures.

It is clear that the tests at 37°C reveal the presence of a variety of the anti Rh agglutinin (anti-Rh) that corresponds closely in specificity to that giving 73 per cent positive reactions with consecutively tested random human red cells.

On incubating Series I at 20°C and Series II at 37°C, almost complete reproduction of the specific temperature effects could be demonstrated (compare Series IA with IID, and Series IIC with IB). Although the nature of the specificity of the agglutinin acting at 20°C could not be determined, it can be stated that it falls in the general group of cold agglutinins as shown by the reactions in Series III.

The specific behavior of the serum at 37°C indicates that this variety of anti Rh agglutinin falls into the group of warm atypical agglutinins of Levine, Katzin and Burnham.⁶ As a practical application the recommendation is made that in cases in which isoimmunization is suspected the modified compatibility test be performed. This consists of incubation of a mixture of the patient's serum and the donor's cells (Group O or the same group as the patient) at 37°C for thirty minutes or longer, followed by light centrifugation and resuspension of the sedimented cells. Under these conditions distinct specific reactions are readily obtained with any serum having warm atypical agglutinins. Furthermore, the less important reactions of the cold agglutinins can be differentiated. By the use of this method

to carry out successful cases by neglecting

*We are indebted to Drs. Shields Warren and E. H. MacMahon for their studies of the gross and histologic specimens. Dr. Warren concluded the predominant picture was one of hemolytic anemia with erythroblastosis foetalis. The presence of leukocytic elements, although not to myeloid metaplasia, did not exclude a leukemic process.

tions at lower temperatures. Obviously, equal significance could not be assigned to the two sorts of agglutinins—warm and cold—in this case.

The three varieties of human anti-Rh agglutinins are discussed by Levine.¹² The standard variety (anti-Rh₁) gives 85 per cent reactions and corresponds closely in specificity with the experimental serum of Landsteiner and Wiener.⁵ The other two varieties, anti-Rh_{1,2} and anti-Rh₂, give 87 and 70 per cent reactions and contain several agglutinins, one of which corresponds to the antibody described in this case.

The inadvisability of giving transfusion after transfusion in a case of acute hemolytic anemia is well exhibited in this case, in which groups of transfusions were given even when the patient's condition was relatively good and the red-cell counts had risen to 2,500,000 and to 3,000,000. Not only did the patient almost succumb when the last group of transfusions were given, but it is possible that an irreversible autohemolytic process became established at this time. Judging from the management of 25 cases of acute hemolytic anemia and hemolytic crisis, it is our belief that if three or four transfusions of blood have been without effect on the hemolytic process, other transfusions will also probably be ineffective, and the advisability of splenectomy should be immediately considered, lest the hemolytic process become permanent or the patient have such severe reactions that splenectomy might become either unwise or ineffective.

The myeloid metaplasia of the liver and spleen in this case was probably the result of severe continuing hemolysis with extreme regenerative activity on the part of the bone marrow and reversion to the potential hematopoietic functions of the liver and spleen. Others, notably Jackson, Parker and Lemon,¹³ have interpreted similar pictures as being due to agnogenic myeloid metaplasia of the spleen with coincidental hemolytic anemia and have pointed to the inadvisability of splenectomy in such a situation. Since the hemolytic process in this case was undoubted and had become aggravated by severe hemolytic transfusion reactions, sufficient reason appeared to be present for the development of myeloid metaplasia. What is more, the contention of Jackson et al. that an agnogenic myeloid metaplasia of the spleen exists is not borne out by our experience, which indicates that for this to develop the bone marrow must become either aplastic, fibrotic, occupied by

foreign tissue or unusually hyperplastic, as in a hemolytic process. Thus in erythroblastosis foetalis, which we consider to be acute hemolytic anemia of the newborn,¹⁴ myeloid metaplasia of the spleen and liver is of common occurrence. The histology of the liver and spleen in the present case resembles closely that seen in erythroblastosis foetalis.

SUMMARY

A patient with subacute acquired hemolytic anemia, when given successive transfusions, finally developed severe and almost fatal hemolytic reactions. Subsequent testing revealed that the patient (Group O, Rh-) had developed isoimmunization to the Rh factor with the presence in the blood of both a warm anti-Rh agglutinin and a cold agglutinin. Transfusions with Rh- blood were without reaction. Splenectomy and biopsy of the liver showed intense myeloid metaplasia of both organs. Death resulted from acute toxic necrosis of the liver, and post-mortem examination also revealed widespread myeloid metaplasia in the presence of severe hemolysis.

Repeated transfusions in cases of acute hemolytic anemia may be followed by isoimmunization and the development of irreversible hemolysis. As a result, splenectomy—which might originally have been curative—may prove ineffective.

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MEDICAL PROGRESS

DIABETES MELLITUS

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THE year 1941 witnessed the first break in the upward curve of mortality from diabetes mellitus in the registration area of the continental United States during the last seven years. The mortality rates from 1935 to 1941 are as follows:

1935	22.2 per 100,000
1936	23.7 per 100,000
1937	23.7 per 100,000
1938	23.8 per 100,000
1939	25.5 per 100,000
1940	26.6 per 100,000
1941	25.4 per 100,000

The explanation undoubtedly lies first of all in the prolongation in the lives of diabetic patients, and secondly in the causes of death of these patients becoming more and more those of the population in general and not specifically related to diabetes. A death from diabetic coma is now a rarity. The possibility exists that statistics of diabetic mortality will not represent in the future so good a guide to the incidence of diabetes in the country as heretofore, because diabetes will be increasingly recorded as a secondary cause of death or, I fear, be totally omitted from the death certificate. For the true mortality among diabetic patients and for the incidence of the disease in the country, it is probable that privately gathered statistics will be increasingly valuable. Perhaps after the war the American Diabetes Association with its growing membership of physicians will attack the problem. That the number of living diabetic patients in the country is rapidly advancing there can be no question. At the George F. Baker Clinic of the New England Deaconess Hospital there were 1831 diabetic admissions in 1941, with a mortality of 1.75 per cent, and 1977 diabetic admissions in 1942, with a mortality of 2.33 per cent. There was no death from diabetic coma.

DIABETIC COMA

Many articles on diabetic coma have appeared, but the data from the George F. Baker Clinic are so extensive and have been so favorable in the last few years that one hesitates to make comparisons where for one reason or another results have not

been so good. On March 30, 1943, there had been 83 consecutive cases of diabetic coma since August 21, 1940, with the carbon dioxide content of the blood 20 volumes per cent or less, without a fatality. The number of such cases reported between August 21, 1940, and July 15, 1942, was 62.¹

A second report² of diabetic coma, with recovery after the administration of 1820 units of insulin, ended with the following comment:

This case teaches again that diabetic coma is a deficiency state, the deficiency being insulin, and that in deep coma of prolonged duration massive doses of insulin are of prime importance. Other supplementary measures, such as artificial warmth, saline infusions, gastric lavage and enemas, while very helpful, take definitely a secondary place to adequate doses of insulin.

It would be wrong to ascribe the success of the treatment of diabetic coma in this clinic to the members of its staff alone. Over and over again in recent months and years the physician outside the hospital, who first recognized the case, has inaugurated aggressive treatment in the home, so that although the patient may have arrived in extremis, a beginning had already been made on which hospital treatment could be built. In proof of the above are the following excerpts from a recent case.

The patient's local physician saw him at 7:00 p.m., diagnosed diabetic coma, recognized the seriousness of his condition, and gave him 70 units of regular insulin. He was admitted to the Deaconess Hospital 1½ hours later.

On admission the patient was completely unconscious and almost moribund, with feeble gasping respirations at 28 a minute, the deep breathing and air hunger that he later recalled having noticed earlier in the day having disappeared. He appeared in a definite state of shock with a blood pressure of 76/40, flushed face, dry tongue and a strong odor of acetone on the breath. The rectal temperature was 92°F., and the pulse 94. The skin was dry and cold. The bladder was distended almost to the umbilicus. The liver was palpable 2 cm. below the costal margin. The lungs were clear and the heart was normal in size. The eyeballs were so soft that the tension could not be measured by an ophthalmologist even 12 hours after entrance. Lipemia retinalis was looked for but not found.

Blood samples for the determination of the sugar level and the carbon dioxide combining power were taken; the patient was covered with several blankets, and four warm water bottles were placed near him, one blanket thickness from the body. The urine gave a red Benedict

*The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, C-8 pp., Springfield, Illinois: Charles C. Thomas Company, 1942, \$5.00).

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test and a ++++ test for diacetic acid, and in consequence 50 units of crystalline insulin was immediately injected.

A preliminary blood-sugar report, 20 minutes after entrance, showed that the blood sugar was above 1000 mg. per 100 cc., whereupon 100 units of crystalline insulin was given intravenously and another 100 units subcutaneously. By this time the final report was ready and showed that the blood sugar was 1230 mg. per 100 cc. and that the carbon-dioxide combining power was 7 vol. per cent.

Huge doses of crystalline insulin were indicated, and therefore within the first 4 hours the patient received 1550 units, 600 of which was given intravenously, the latter because of his poor circulation and obviously poor chance for its quick absorption. By the end of 5½ hours of hospital treatment he had received 1750 units of insulin, to which should be added the 70 units given by his local physician 1½ hours before admission, making a grand total of 1820 units in 7 hours. No more insulin was administered for the next 17 hours.

It is most unlikely that this patient would have survived without having received the original 70 units of insulin an hour and a half before his hospital admission. It is quite possible that 10 units given early equals 100 units after an interval of two or three hours — "a stitch in time saves nine."

In this connection, it should be restated that in the George F. Baker Clinic a case is reported as a coma death if the patient is admitted to the hospital in coma, even if he does not die for days or weeks after recovery from coma. Only in this way is one sure to obtain the true mortality from coma. Not uncommonly a patient may temporarily recover, but the treatment given for the coma may have so injured the liver or some other organ or part of the body that, although death did not actually result from coma, it was a direct sequence of it, either immediate or remote.

DIABETIC CHILDREN SURVIVING TWENTY YEARS

Insulin was first administered clinically in 1922. Between 1914 and 1922 the average duration of life of the diabetic child did not exceed two years. It was, therefore, appropriate for Eisele³ to report from the George F. Baker Clinic 73 patients with diabetes with onset under fifteen years of age who had survived twenty years or more. Seventy-one of these were still living. In March, 1922, there were but 103 living children in this clinic, and the 73 who lived twenty years or more represent 72 per cent of this number. Of the 2 who died, one succumbed at twenty-nine years of age to septicemia following an upper respiratory infection, and the other, with a history of onset in 1886 at the age of eight, died in coma twenty-nine years later, in 1915. Fifty-five per cent of the patients were males. The average age at onset of the diabetes for this group was 9.0 years for the males and 8.7 years for the females. The young-

est patient developed diabetes at one year and seven months. The oldest living patient is now forty-one, representing the only one living in the fifth decade; there are 39 in the fourth and 31 in the third decade. On the average, the group showed diabetes for 2.8 years before insulin became available. Heredity was positive in 62 per cent, the highest percentage of heredity yet reached by any group save homologous twins, in which the incidence has been recorded as 63 per cent.

The early appearance of arteriosclerosis was the most important complication. Thirty per cent of the series who were examined roentgenologically showed it, and among 55 per cent of those examined there was moderate to advanced ocular sclerosis. Among these two groups, 70 per cent had either hypertension or albuminuria or both at an average age of twenty-nine years.

Impaired physical development in childhood occurred in 16 per cent of the series. However, the average male adult weighed 146 pounds and was five feet, seven inches and the average female weighed 127 pounds with a height of five feet, four inches. Infections played a relatively minor role in the lives of these patients, and operative procedures were done with little more hazard than in patients in a nondiabetic group.

The educational achievement of those who make up this series is probably the most striking feature brought out in the study: 42 per cent have attended college, as compared to 7 per cent of the population of the continental United States who are twenty-one or more years of age.

DIABETIC DWARFISM

From the George F. Baker Clinic, Wagner, White and Bogan⁴ reported the occurrence, classification and management of diabetic dwarfism. The incidence of retardation among 1407 diabetic patients with onset of the disease under fifteen years of age was 8.3 per cent. The characteristics of 4.6 per cent of the entire series of juvenile diabetic patients and 55 per cent of the retarded group were stunted stature, abnormal proportions, delayed differentiation and hypogenitalism. The remainder of the retarded children were classified as follows: transitory infantilism, 27.1 per cent; constitutional dwarfism, 11.9 per cent; undernutrition, 2.5 per cent; congenital anomalies, 1.7 per cent; neglect, 0.9 per cent; and tertiary syphilis, 0.9 per cent. Thyroid extract, parenteral anterior-pituitary extract and testosterone stimulated growth in typical diabetic dwarfism. The increased severity of diabetes that followed endocrine therapy was evaluated. The social and economic importance of the problem was believed to outweigh the danger resulting from increase in severity of dia-

betes, which, after all, was controlled by an increase in the prescribed amount of insulin.

The acceleration of growth, the early onset of puberty and the sexual maturity at the onset of diabetes in childhood were re-emphasized by these authors. The tendency for a decrease in the rate of growth—the occurrence of leanness in boys and obesity in girls in adolescence—during prolonged duration of the disease was reported. Fischer, Mackler and Marks⁵ confirmed these observations.

Vitamin deficiencies in diabetic children are reported in 26.8 per cent of the children observed in the camp of the New York Diabetes Association. Freston and Loughlin⁶ found vitamin B deficiency commonest. Deficiency of vitamin A or C was usually accompanied by that of other vitamins. Chemical determinations for carotene were normal. Levels for vitamin A or C or both were low in 88 per cent of the cases tested. Poorly controlled diabetes and hepatomegaly were found in those patients who had signs of vitamin deficiency.

TWO-DOSE GLUCOSE-TOLERANCE TEST

A careful re-evaluation of the two-dose glucose-tolerance test was made by Wayburn and Gray.⁷ Obesity was found to impair the ability of patients to endure the strain of the double load imposed by the two-dose test. There was a close relation between values of the blood sugar and the amount of glycosuria. The one-hour blood-sugar value was found to be the best single determination in the diagnosis of diabetes, and the two-hour value in the classification of its severity. Those authors state that the two-dose glucose-tolerance test is relatively free from the influence of the preceding diet so commonly a disturbing factor in a two-hour, single-dose test.

ETIOLOGY

Anticipation in the pattern of inheritance in diabetes has been re-emphasized by Woodyatt and Spetz⁸. Colwell⁹ promulgates the optimistic theory that diabetes mellitus begins at birth, that inherent features predetermine the average rate of its progress, that its course is approximately half run before the disease is even recognized, and that some years after recognition it may show progressive and permanent improvement.

ADRENAL GLAND IN CARBOHYDRATE METABOLISM

Evidence pointing to the importance of the adrenal gland in carbohydrate metabolism has advanced considerably in the last few years. Since 1901 it has been known that the medulla was implicated, but of late the greater role of the cortex

has been recognized. Before presenting a review of recent articles, a brief summary of the action of the two anatomic divisions of the adrenal glands may not be out of place.

Adrenalin, the active principle of the adrenal medulla, obtained by Takamine and Aldrich in 1901, when injected subcutaneously into an animal, as first noted by Blum in 1901, leads transitorily to hyperglycemia and glycosuria. This is accompanied by the conversion of glycogen in the liver into sugar and its discharge into the blood stream, thus opposing insulin, which promotes the formation of glycogen in the liver and muscles. The hyperglycemia produced by adrenalin is greatest when the hepatic store of glycogen is at a maximum, as in well-fed animals, whereas in a hepatectomized animal hyperglycemia fails to appear. Adrenalin likewise reduces the glycogen of the muscles. The muscle glycogen is broken down into lactic acid, which in turn is resynthesized in the liver to glycogen, and this glycogen can again be converted into glucose and subsequently taken from the blood stream and can re-form muscle glycogen, thus completing the cycle. When adrenalin is given after a prolonged fast, or when the hepatic glycogen is low, its effect is to increase the glycogen reserve. The antagonism between adrenalin and insulin has long been known and in 1907-1908 was studied by Zuelzer, who went so far as to designate as a unit that amount of the antidiabetic substance in his extract of the pancreas that would prevent the glycosuria caused by the injection of 1 mg. of adrenalin. In fact, today a 1:1000 solution of adrenalin in 0.5-cc. or 1.0-cc. doses is often employed to counteract the hypoglycemia of an insulin reaction. Hypoglycemia was first noted in Addison's disease by Porges in 1910. Diabetes is never produced by adrenalin, and removal of the medullas from both adrenals does not ameliorate diabetes or prevent its appearance when the pancreas is subsequently removed.

Unlike the medulla, the cortex of the adrenal gland is essential to life, and death in ten to fifteen days follows removal of more than about five sixths of the gland. Pregnant animals (the cortex enlarges during pregnancy) and those in heat survive such removal longer. Various hormonal principles are concerned; among these are hormones controlling the distribution of inorganic ions and the permeability of membranes, and others that affect glucose formation and the deposition of glycogen in the liver. Desoxycorticosterone belongs to the former group and has no effect on carbohydrate metabolism, whereas the latter hormones belong to the corticosterone series, similar chemically to the sex hormones, and

control not only carbohydrate metabolism but also the electrolyte balance.*

In 1934 and 1935, Long and Lukens showed that cats and dogs after combined adrenalectomy and pancreatectomy might be kept alive for considerable periods—from eight to thirty-five days—with only slight glycosuria. Ketonuria did not appear. On the other hand, the administration of cortical hormone led to an increase in glycosuria.

In adrenal insufficiency, carbohydrate metabolism is disturbed in three ways: there is an increased oxidation of glucose in the peripheral tissues (muscles); the liver and kidney fail to synthesize glucose from tissue protein, amino acids and lactic and pyruvic acids; and hypoglycemia is present, as well as a failure of the liver to convert glucose to glycogen. Thus a deficiency of the adrenocortical hormones lowers the supply of energy available for the needs of the body: in consequence, the muscles become incapable of performing work, the liver ceases to carry on its normal carbohydrate function, and the kidney fails in some of its activities. If, on the other hand, extracts of the adrenal cortex containing the essential cortical hormones are administered, the reverse of these actions takes place both in the normal and the adrenalectomized animal.

In 1930, Swingle and Pfiffner extracted a substance from the adrenal cortex that, when injected, counteracted the removal of the adrenals, and animals so treated survived indefinitely. Hartman obtained an extract that he called cortin. Subsequently Grollman and Firor obtained a much more potent extract with the help of acetone. Long demonstrated in 1936 that hypoglycemia could be produced by adrenocortical insufficiency, and this was also observed by Grauman in 1938. Kendall and also Reichstein have isolated several closely related steroids, and to one of these, which was peculiarly active in crystalline form, Reichstein gave the name "corticosterone" and assigned it the following formula: $C_{21}H_{28-30}O_4$. This substance when made synthetically has one less oxygen atom and is called desoxycorticosterone.

The diabetes of a depancreatized animal if adrenalectomized is rendered mild in a manner analogous to what occurs when a depancreatized animal is hypophysectomized. Conversely, Hartman's extract of the adrenal cortex, cortin, given to a normal animal raises the blood sugar and increases the deposition of glycogen. The alleviation of the diabetes in a depancreatized rat as a result of adrenalectomy is due to the absence of cortin, which is diabetogenic, and, in fact, such animals if kept alive by sodium chloride are not

diabetic. The administration of cortical extract, corticosterone, dehydrocorticosterone or Kendall's Compound E to either fasted normal or adrenalectomized mice and rats is followed by large increases in liver glycogen and slight hyperglycemia. Over the course of a few hours adrenocortical extract may thus increase the blood sugar by more than 100 per cent.¹⁰ It is also effective by mouth in raising blood-sugar levels. At first it was thought that the gluconeogenesis from protein was of sufficient magnitude to account for all this newly formed carbohydrate, but later work tends to disprove this explanation and to suggest there must be another source, perhaps secondary to failure of carbohydrate utilization. Studies on rat-liver slices likewise indicate that the rate of synthesis of carbohydrate from pyruvate and *D*-lactate is markedly increased by adrenocortical hormone.¹³

In adrenal insufficiency carbohydrate absorption is reduced, and this reduction combined with a possible increased utilization may account for the flattened dextrose-tolerance curves found in patients with Addison's disease.¹⁴

Adrenocortical hormone favors glycogenesis in the liver, whereas desoxycorticosterone does not. In Bloomfield's¹⁵ case of Addison's disease, desoxycorticosterone acetate failed to produce an increase of blood sugar or glycosuria, a conclusion similar to that reached by McGavack, Charlton and Klotz.¹⁶ Eschatin, on the other hand, administered in large doses for three days did do so. In contrast, insulin may affect favorably the formation of glycogen in muscle.

As a matter of fact, the occurrence of diabetes in association with Addison's disease is rare. Rhind and Wilson¹⁷ found 14 cases in the literature but had doubts regarding 5 of them. A feature of these cases has been their insulin hypersensitivity.

The oral administration of a hormone, according to Grollman,¹⁸ has advantages over the parenteral route in that it simulates more closely the normally continuous passage of the hormone from the gland. Its expense, however, makes it prohibitive.

The manner in which the cortical principles inhibit the utilization of carbohydrate is not known.

Shipley and Fry¹⁹ in 1942 made a special study of the effect of an adrenocortical ketosis and demonstrated that adrenocortical extract, corticosterone, desoxycorticosterone and 11-dehydro-17-hydroxycorticosterone played no part in ketogenesis. Estrogens, which are similar in structural outline to the cortical hormones, increase liver glycogen and the nitrogen excretion of fasted rats, and this is attributed to stimulation of the

*For recent summaries of problems relating to the adrenal cortex, one should refer to Long's¹⁰, ¹¹ and Ingles's¹² comprehensive articles, of which the latter contains one hundred and forty-six references to the literature.

adrenal cortex by their action on the anterior pituitary gland, since they do not produce these effects in adrenalectomized and hypophysectomized animals. The anti-insulin effect of the anterior pituitary, according to Grattan, Jensen and Ingle²⁰ is mediated through the adrenal cortex and does this by promoting the formation of glycogen. However, Long et al.²⁰ do not believe that the diabetogenic hormone of the pituitary gland is entirely mediated through the adrenal cortex, but rather that a synergism exists between the two hormones.

In connection with studies on rats deprived of the pituitary gland or adrenal medulla, Gellhorn, Feldman and Allen²¹ assayed the insulin in the blood. In their investigation they used rats deprived of the pituitary gland, rats deprived of the adrenal medullas and rats deprived of both. Space does not permit the giving of details. Insulin was injected intraperitoneally, and sixty minutes after injection the percentage of sugar in the blood was determined. Tests were made both with insulin and with blood. By this means these authors determined that the insulin content of normal human blood is approximately 0.0002 unit per cubic centimeter; that is, in 5000 cc. of blood, the blood content of the human body, the amount of insulin would be 1 unit. In normal dogs fasted for twenty-four hours the blood contained 0.0001 unit of insulin per cubic centimeter, or half as much. Another conclusion from this study was that the only source of insulin that appears in the blood is the pancreas.

Ingle^{22, 23} produced glycosuria in normal rats with a forcibly fed high-carbohydrate diet by the injection of large amounts of 17-hydroxy-11-dehydrocorticosterone. Hyperglycemia, the increased excretion of nonprotein nitrogen, marked loss of weight and atrophy of the testes and thymus gland were also observed. Ingle also tested the diabetogenic effect of stilbestrol in forcibly fed normal and partially depancreatized rats, and noted that very small doses were effective in increasing the severity of the diabetic state of the partially depancreatized animals. Doses of 2 gammas and 10 gammas exerted as positive an effect as did larger doses. Since stilbestrol is estrogenic in amounts as small as 0.5 gamma per day, it is apparent that it is a highly active compound from both the physiologic and pharmacologic standpoint. The four estrogens studied manifest diabetogenic activity in smaller doses than do testosterone and methyltestosterone.

In a comprehensive review of problems relating to the adrenal cortex, Ingle¹² states that adrenocortical insufficiency is characterized by hypoglycemia and the depletion of tissues and carbo-

hydrate stores, especially during fasting; secondly, even in animals depancreatized or treated with phlorhizin the glycosuria is diminished by removal of the adrenals; thirdly, in adrenalectomized animals there is diminution of the formation of carbohydrate from protein, as shown by reduction of urinary nonprotein nitrogen; and, fourthly, in such animals there is an abnormal sensitivity to insulin. All these changes can be reversed by treatments with cortical extract, corticosterone, 11-dehydrocorticosterone, 17-hydroxycorticosterone and 17-hydroxy-11-dehydrocorticosterone. The deficiencies in carbohydrate metabolism can be restored to normal by injection of these substances, and, moreover, carbohydrate stores of blood and tissues can be raised above normal both in these and in adrenalectomized animals. Finally, the diabetogenic effect is so marked that partially depancreatized rats that show no spontaneous glycosuria can be made to excrete all the available carbohydrate of the diet during the administration of these cortical principles.

The observation of Ingle that normal rats can be made severely diabetic by the administration of 17-hydroxy-11-dehydrocorticosterone has not yet been independently confirmed. Either normal or adrenalectomized animals become abnormally resistant to the convulsive effect of insulin during treatment with the C-11 oxygenated cortical steroids.

Conn and Conn,²⁴ in an organic case of hyperinsulinism, found no apparent anti-insulin effect or blood-sugar-raising effect from the daily administration of 30 cc. of adrenocortical extract. They go on to say that the amount of this material used to produce a rise in the blood sugar is relatively so large that it may represent a response that is possible only under distinctly abnormal circumstances, and the clinical use of the material is impractical as an insulin antagonist with the adrenocortical extracts now available.

The oral administration of diethylstilbestrol was tested by Allen and Bern²⁵ with guinea pigs of both sexes, and definite enlargement of the adrenal cortex was observed.

Janes and Nelson²⁶ formulated a theory to explain why diethylstilbestrol raises the level of the carbohydrate in the rat. Since it is ineffective in either adrenalectomized or hypophysectomized animals, they infer that one or the other of these glands must be involved. They suggest that diethylstilbestrol stimulates the hypophysis to release some factor, possibly adenotrophic hormone, which in turn stimulates the adrenal cortex to produce a considerable quantity of some cortical hormone or hormones that are characterized by

having an atom of oxygen attached to the eleventh carbon atom. Such hormones are effective in promoting glycogenesis and deposition of glycogen in the livers of fasting animals.

Kenyon et al.²⁷ failed to note a change in blood glucose in a patient who was given testosterone, nor was the slight glycosuria increased. They saw no indication of the diabetogenic properties in testosterone propionate, that had been described by Ingle,²² using massive doses in the partially depancreatized rat on a high-carbohydrate diet, or of those described by Dolin, Joseph and Gaunt²⁸ in the partially depancreatized ferret.

The influence of traumatic shock on the blood sugar of adrenalectomized rats treated with adrenocortical extract was studied by Selye and Dosne.²⁹ Trauma failed to elicit hyperglycemia when the adrenals were absent. When an active cortical hormone was injected into such animals during trauma, a significant rise in the blood sugar occurred and at the same time an increase in resistance to shock.

A clinical case of the association of tumor of the adrenal cortex with diabetes has been reported by Sprague, Priestley and Dockerty.³⁰ The diabetes of a forty-nine-year-old woman with no diabetic heredity was discovered in 1938. The disease was difficult to control and required protamine-zinc insulin and crystalline insulin up to 125 units daily, without hypoglycemia. There was no acidosis. The fasting blood-sugar level was 375 to 250 mg. per 100 cc. The diet contained 146 gm. of carbohydrate; the blood pressure was 160 systolic, 94 diastolic. In the right upper quadrant of the abdomen, a large, movable mass was palpable. There was no abnormality of the genitalia or secondary sex characteristics. In March, 1941, the mass, which was then the size of a football, was removed. The fasting blood-sugar levels on the third and fifth postoperative days were 107 and 88 mg. per 100 cc., respectively. There was no glycosuria. Insulin was discontinued. On the twenty-fifth postoperative day, an Exton-Rose glucose-tolerance test was carried out with 50 gm. of glucose given fasting and 50 gm. in thirty minutes. Neither the fasting urine nor the urine in sixty minutes showed glycosuria, and the blood-sugar levels fasting, in thirty minutes and in sixty minutes were 85, 122 and 144 mg., respectively. Eighteen months later the patient was still sugar free. Apparently this patient with an adrenal tumor but without other endocrine manifestations secreted only the cortical steroids controlling carbohydrate metabolism.

In 1936, Long³¹ discovered evidence of impaired carbohydrate metabolism in half of 55 reported cases of adrenocortical tumor.

PREGNANCY

White and Hunt³² state that the problem of pregnancy complicating diabetes is controversial in four primary respects. First, as regards fetal survival, they ask, Does it deviate significantly from the normal? Secondly, as to the characteristics of the infants of diabetic mothers, is there an infant recognizable as one so produced? Thirdly, as to the clinical course of the mother, is it normal or abnormal, and does it affect the fetus? Fourthly, what is the need for special care of the infant and the mother?

Between January, 1936, and July, 1942, one hundred and twenty-five consecutive pregnancies occurred in 119 different diabetic patients. In 92 per cent of the patients the diabetes was well established prior to the onset of pregnancy, and in only 9 per cent was the diagnosis made during pregnancy.

Maternal mortality was not the problem. There was 1 death, a mortality of 0.8 per cent. Seventeen of the fetuses died, making the fetal mortality 12 per cent. The causes of death were as follows: macerated stillbirth in 6 cases, atelectasis in 6, subtentorial hemorrhage in 2, hemorrhagic disease of the newborn in 1, defect of the skull in 1, and erythroblastosis in 1. Comparable diabetic fetal mortality has varied from this level to as high as 35 per cent, even in the recent reports of Lawrence and Oakley³³ and of Barns,³⁴ and if one studies the entire forty-week period of pregnancy, it has been as high as 50 per cent.

Characteristics of the infants of diabetic mothers were as follows: oversize was a predominant trait in this series, 80 per cent of the infants exceeding the expected weight for age. Weight was influenced by three factors: body fat, edema and splanchnomegaly. The edema was sometimes visible, sometimes manifested by weight loss, which was excessive, and sometimes manifested through spontaneous diuresis. The enlargement of the organs was most striking in the liver, spleen and heart, less so in the lungs and kidneys, and variable in the pancreas and thymus and adrenal glands.

The significant pathologic changes were as follows: excessive hematopoiesis of the liver and spleen resembling that found in erythroblastosis occurred in 14 of 17 autopsied infants, atelectasis in 13, persistence of fetal glomeruli in 6, and hyperplasia of the islets in 5. Hertig³⁵ has reported glycogen infiltration of the enlarged heart and Brenner³⁶ follicular maturation, corpora hemorrhagica and luteinization in the ovaries of female infants of diabetic mothers.

Congenital defects were found in 17 per cent of the 125 cases. They were usually slight, and most often involved the mesenchymatous tissue.

Clinical behavior was characterized by respiratory difficulty, fever, instability, jaundice and difficulty in feeding. Self-correcting hyperglycemia and hypoglycemia were often observed.

The maternal course was abnormal. Forty-two per cent of the 125 mothers had toxemia, and 25 per cent delivered prematurely. Only 0.8 per cent had diabetic coma, and only 0.8 per cent had severe hypoglycemia.

One of three patterns of behavior was observed in abnormal pregnancies: weight gain, edema, hydramnios, albuminuria and hypertension with intrauterine deaths; hydramnios with intrauterine death; and premature delivery and neonatal death without signs of toxemia.

Fetal wastage and an abnormal clinical course could not be correlated with congenital defects or the disturbed chemistry of diabetes, but both occurred with an imbalance of the hormones of pregnancy.

Forty-one of the patients had a normal balance of the hormones of pregnancy and 84 had an abnormal balance. Of the latter, 27 had no corrective treatment and 57 had substitutional estrin and progesterin therapy.

When the hormonal pattern was normal, the fetal survival was 95 per cent (39 of 41 cases), the incidence of toxemia 2 per cent, and premature delivery zero. When the pattern was abnormal, the uncorrected fetal survival was 60 per cent (17 of 27 cases), toxemia 52 per cent, and prematurity 40 per cent. When corrective treatment was employed, the toxemias were modified, fetal survival was 92 per cent (52 of 57 cases), and prematurity was 18 per cent. Diethylstilbestrol in doses from 10 to 50 mg. daily and proluton in doses from 5 to 40 mg. daily were used most commonly. The dosage depended on the response of the level of serum chorionic gonadotropin and urinary pregnanediol.

Forty per cent of these patients were delivered normally, 60 per cent by cesarean section. Premature delivery of abnormal cases is recommended by White, with the date of choice the thirty-seventh week.

Oxygen incubation, heat and dehydration were used routinely for the abnormal infants.

From this study, it appeared that when pregnancy complicated diabetes fetal survival deviated significantly from normal, and there was a factor lethal to the infant.

An infant characteristic of the diabetic mother was observed. The picture could be explained

more adequately on the basis of a disturbance of sex hormones than on the basis of diabetes.

The clinical course of the mother was abnormal, being characterized by toxemia and premature delivery associated with stillbirth and neonatal death. These abnormalities were predictable and probably caused by an imbalance of the sex hormones. Corrective substitutional therapy modified the abnormal maternal course and raised fetal survival to more than 90 per cent.

BLOOD PYRUVATE AND LACTATE

In normal persons the ingestion of glucose is always followed by a rise in blood pyruvate, as shown by Bueding, Fazenkas, Herrlich and Himwich,³⁷ Bueding, Stein and Wortis³⁸ and Stotz and Bessey.³⁹ The rise usually reaches a maximum at the end of one hour and returns to a normal fasting range of 1 mg. per 100 cc. at the end of three hours. The average maximum in 27 normal subjects reported by Bueding, Wortis and Fein⁴⁰ was 1.5 mg. Stotz and Bessey have considered that this rise in pyruvic acid following ingestion of glucose is reliable evidence of an increase in glucose combustion. According to Klein,⁴¹ fasting pyruvate levels were normal in 27 of 28 diabetic patients and the lactate was normal in 23 of 25. Following the administration of glucose without insulin a delayed slight rise in pyruvate occurred with no increase in blood lactate. When both insulin and glucose were administered, significant increases in both pyruvate and lactate occurred. So far a comparison of the rise in blood pyruvate and the increase in blood lactic acid with the changes in the respiratory quotient that follow the ingestion of glucose has not been reported. Studies carried out at the George F. Baker Clinic⁴² this year in co-operation with the Nutrition Laboratory of the Carnegie Institution of Washington and Dr. Elmer Stotz of the Department of Biological Chemistry, Harvard Medical School, were designed, first, to see whether a close correlation existed between the changes in respiratory quotient and the changes in blood pyruvate.

A second important cause of alteration in the blood lactate-pyruvate relation is found in thiamin deficiency. Thus, Stotz and Bessey³⁹ have reported data both in human beings and in rats that show that the parallel relation between the levels of blood lactate and of blood pyruvate does not hold when the quantity of lactic acid in the blood is above or below 20 mg. per 100 cc. In thiamin deficiency the rise in blood pyruvate above the fasting level is often excessive. In a diabetic patient studied this winter the fasting blood pyruvate was 0.6 mg., and the value rose

to 2.8 mg. after she received glucose. At the same time the blood lactic acid rose from the basal value of 3.8 to 25.3 mg. This patient had had nausea and vomiting constantly for three weeks owing to uncontrolled diabetic acidosis. The possibility existed in this case that some degree of thiamin deficiency was present.

Another object in this study was to compare the results obtained in diabetic patients with and without the use of insulin. Bueding, Wortis and Fein⁴⁰ found that in diabetic patients the ingestion of glucose was followed by little or no increase in blood pyruvate. Yet when insulin was given, a very significant rise in blood pyruvate occurred. Bueding, Fazenkas, Herrlich and Himwich³⁷ injected glucose into normal animals by the intravenous route at the rate of 2 gm. per kilogram of body weight. In depancreatized dogs no rise in blood pyruvate occurred. However, in such dogs, when insulin was administered simultaneously, a marked rise in pyruvate occurred. It was also noted, however, that without insulin when the blood-sugar level was raised from 750 to 950 mg. per 100 cc., an increase in blood pyruvate might occur even without insulin.

A group of 22 diabetic patients and 1 normal subject were studied at the George F. Baker Clinic. In the majority of patients, observations were made on two different days, on one with insulin administered intramuscularly at the same time glucose was given by mouth and on the other without insulin administration. In general, little or no rise in blood pyruvate and blood lactate occurred following the administration of 50 gm. of glucose by mouth without insulin. Usually little or no rise in the respiratory quotient occurred under these circumstances. On the other hand, when insulin was given at the same time as glucose, a striking rise both in the respiratory quotient and the blood pyruvate and lactate took place. The correlation seems well established.

On the other hand, there were 2 patients, a young diabetic man and a mild diabetic woman who had had a thyroidectomy, in whom a considerable rise in the respiratory quotient was observed with a slight, almost negligible, rise in the blood pyruvate and lactate. It is tempting to consider the possibility that in these patients some glucose was oxidized directly without the intermediary stage of pyruvic acid formation. However, Stotz would consider this too speculative in view of the fact that in more than 90 per cent of the group the correlation between a rise in the respiratory quotient and the change in the blood pyruvate and lactate was so close.

In the group studied is included a patient who was in hypoglycemia during the latter part of the

metabolism study. The fasting blood-sugar value was 65 mg. per 100 cc. on the day when he received 20 units of insulin in addition to 50 gm. of glucose, and 59 mg. on the day when he received glucose only. His fasting basal respiratory quotients were 0.94 and 0.89 respectively. When he received glucose only, there was no significant rise either in the respiratory quotient or the blood pyruvate, but when he received 20 units of insulin as well as 50 gm. of glucose, the respiratory quotient rose from 0.94 to 1.04.

One patient was studied following the administration of levulose, and it was found that a rise of 0.07 in the respiratory quotient occurred and simultaneously the blood pyruvate rose 0.5 mg. per 100 cc. Further observations are being made with the hope that some further information about the effects of levulose in diabetes may be obtained.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 29201

PRESENTATION OF CASE

A seventy-seven-year-old housewife was referred to the hospital because of attacks of severe upper abdominal pain.

Four and a half months before admission the patient first experienced severe sharp pain, like a constricting band, that began at the right costal margin and radiated across the abdomen to the left upper quadrant. This lasted several minutes and then spontaneously cleared when she was propped up in bed. Similar attacks recurred that varied in degree, but bore no apparent relation to activity, meals or diet. The patient was able to carry out her normal duties effectively except during an attack. Recently she believed that the abdomen had become more protuberant. There was no history of nausea, vomiting, jaundice, diarrhea or tarry, bloody or acholic stools. The genitourinary and cardiac histories were not remarkable. The patient was said to have lost 23 pounds during the two years prior to admission.

The past history was not remarkable. A sister died of cancer of the uterus.

Physical examination revealed a fairly well-developed and well-nourished woman who seemed comfortable. The heart and lungs were normal. The abdomen was distended, and there was a slightly tender, round, grapefruit-sized mass in the left upper quadrant extending from the costal margin to a point 2 cm. below the level of the umbilicus. This did not seem to be attached to the liver and did not move with respirations.

The blood pressure was 190 systolic, 90 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 11.3 gm. and a white-cell count of 9100, with 82 per cent neutrophils, 14 per cent lymphocytes, 1 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. The urine was normal. A blood Hinton test was negative. The nonprotein nitrogen was 16 mg., and the protein 6.7 gm. per 100 cc.; the chloride was 97.5 milliequiv. per liter.

A chest roentgenogram showed slight atelectasis of both lower lung fields, which was more marked

on the left. The heart appeared to be within the upper limits of normal. The aorta was tortuous and slightly calcified in the arch. An intravenous pyelogram demonstrated normal kidney outlines; no definite stones were seen. There was a large soft-tissue mass in the left midabdomen that filled the flank and extended downward to the level of the left iliac crest (Fig. 1). Intravenous dye appeared promptly and outlined nondilated urinary passages. A barium enema passed to the cecum without delay. The huge mass in the left upper quadrant displaced the colon posteriorly and downward. The appendix lay well up under the right colon. No definite evidence of intrinsic disease within the bowel could be demonstrated. A barium meal outlined a normal esophagus. The stomach was low in position and was displaced to the right and anteriorly by a soft-tissue mass 20 cm. in diameter that occupied almost the entire left side of the abdomen. The stomach was adherent to the mass over the middle half of its length, and one portion was flattened along the surface of the mass. No definite ulceration was demonstrable and the mucosa was apparently uninvolved. The third portion of the duodenum and the adjoining jejunum were displaced medially.

On the day after admission, the patient had a typical attack of pain, which lasted several minutes and disappeared when she was propped up in bed. The abdomen was exquisitely tender in the region of the mass. Normal peristalsis was audible during the attack, and the patient was not nauseated and did not vomit.

An operation was performed on the ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. MERRILL C. SOSMAN†: On physical examination the mass in the abdomen was described as grapefruit sized. This is a conservative estimate of the size of the mass—either a conservative man described it, or a man from California, who is accustomed to large-sized things of all kinds. It is much larger than a grapefruit—over 20 cm. in diameter in the x-ray film.

Older people who lie in bed for a considerable length of time are prone to get small areas of atelectasis in the lung bases, but sometimes we are unable to see them because of the elevation of the diaphragm, particularly in an adipose patient with a protuberant abdomen. There is a triangular area here in the left base. As a rule these atelectatic zones are parallel to the diaphragm and may have a prominence at the lateral end. It may be a triangle simulating a small pulmonary

*On leave of absence.

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infarct, which also frequently occurs in the base. More important is the fact that the rest of the lungs are clear. There is no evidence of metastases, and no elevation of the left half of the diaphragm, which one would expect if this large

The barium enema is negative except for the displacement of the splenic flexure, which is lower than the hepatic flexure. The description of the fluoroscopist says that it was "displaced posteriorly as well as downward." I am thinking of two pos-

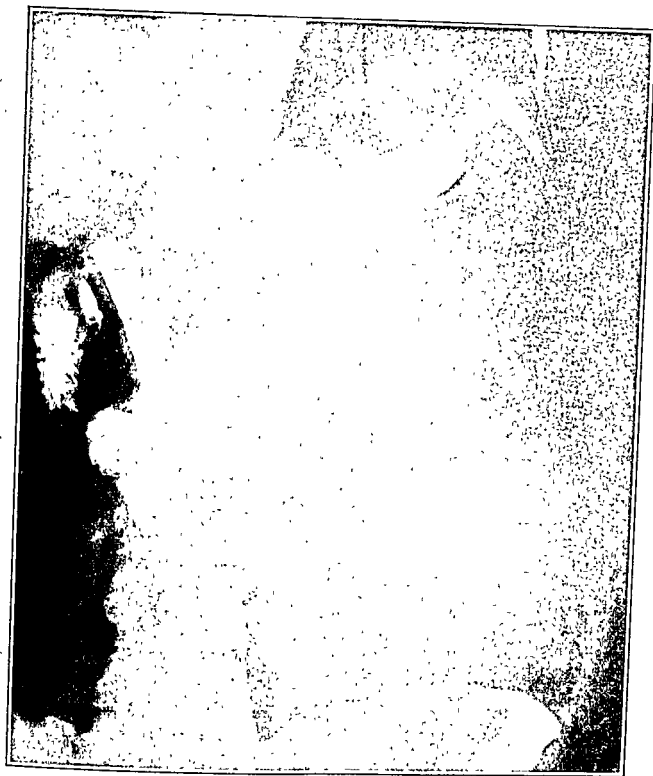


FIGURE 1. Roentgenogram following a Barium Meal, Which Shows a Large Soft-Tissue Mass in the Left Midabdomen That Displaces the Stomach.

mass were the spleen. The entire left kidney is well outlined, the lower pole being easily visible through the upper edge of the mass. There is no distortion of the renal pelvis, such as one would expect if this were an intrinsic tumor of the kidney. Occasionally, tumors of this size are primary in the kidney, such as benign adenomas, but they always distort the renal pelvis. The only other tumor of the kidney of this size would be a benign cyst. This usually has a pedicle attached to the kidney, but does not distort the kidney pelvis or the kidney outline.

sibilities: one, a large tumor of the tail of the pancreas, and the other, a huge tumor arising in the wall of the stomach, an extramucosal tumor. Tumors arising in the stomach wall ordinarily displace the colon backward, whereas pancreatic tumors are likelier to displace it laterally and perhaps forward. The displacement of the splenic flexure backward favors a tumor arising from the stomach itself.

I think we can rule out tumor of the kidney. I think we can rule out mesenteric cyst. The mesenteric I think is a circular in

outline, do not displace the stomach in this manner or shape and are more or less posterior to the stomach. And I think one can say this mass is adherent to the stomach over a considerable area. When I first saw this film I thought that this triangular projection from the posterior wall of the stomach probably ran into the mass of tumor. In other words it looked like a funnel-shaped projection into the hilum of the tumor. If that were true it would make a fairly definite case for one of the large tumors of the stomach wall—a leiomyoma or one of the less-differentiated spindle-cell tumors, usually a sarcoma. But another possibility is present—namely, that there simply was an adhesion to the stomach wall, which was stretched around the surface of the tumor. The mobility is another important point. These tumors of the stomach, particularly the huge sarcomatous type of tumor, usually can be moved around the abdomen without much difficulty. As one would expect, primary tumor in the pancreas is much more fixed and less movable. Could we find out if the mass showed any particular mobility?

DR. TRACY B. MALLORY: Mobility was not mentioned in any of the notes.

DR. SOSMAN: It says that the mass "did not move with respirations." It does not say whether it could be moved manually. I assume from that that it was at least not freely movable. This is a fairly important differentiating point. At least it has been in the few of these rare tumors that I have seen. I do not believe I can do any better in the differential diagnosis than to say that the two main possibilities here are a primary tumor of the tail of the pancreas—and tumor that big in the pancreas is apt to be degenerated in the center and more or less cystic—and a tumor of the spindle-cell type, either a fibrosarcoma or a leiomyosarcoma, primary in the wall of the stomach. If the mass were freely movable, I should bet on the stomach; and if practically fixed, on a tumor of the tail of the pancreas.

DR. MALLORY: I do not believe there is anyone here who would have an opinion on that.

DR. AUGUSTUS ROSE: What was the mechanism of the pain?

DR. SOSMAN: I should imagine that the huge mass pressing on some of the vessels, mesenteric vessels or aorta, would produce it. When the patient sat up and relieved the pressure the pain disappeared.

DR. RICHARD SCHATZKI: If this were pancreas would you expect it to be a tumor or a cyst of the pancreas?

DR. SOSMAN: A cyst; but they frequently start as adenomas and degenerate in the center, with

a large necrotic area and a little tumor around the wall.

DR. SCHATZKI: Would you expect so much adherence to the stomach as you describe?

DR. SOSMAN: They may be adherent if they become necrotic and develop an inflammatory process in the capsule. One would have to assume that it was necrotic, inflamed and adherent secondarily. The displacement of the duodenal loop to the right,—here is the duodenojejunal junction, and the descending duodenum comes down here perpendicularly to the center of the spinal column,—fits in more with a tumor well posterior in the region of the tail of the pancreas.

This peculiar coarse mottling of the vertebrae is of no clinical importance. I looked at the spine to be sure there were no metastases, and I saw these coarse striations, particularly in the twelfth thoracic vertebra. It might be a benign cavernous hemangioma of the bone, which is of no more importance than a birthmark in the skin, or it might be the early phase of Paget's disease—a coarse trabeculation without much increase in density.

DR. SCHATZKI: What do you think of the posterior displacement of the colon?

DR. SOSMAN: It worries me if I am going to call the lesion a tumor of the pancreas. That fits in better with a tumor of the stomach wall. I cannot on the available evidence decide between the two possibilities.

DR. WILLIAM B. BREED: Does the actual size help differentiate the two possibilities?

DR. SOSMAN: I do not believe so. Either one could become unusually large, either by degeneration and necrosis of the central portion or by edema and swelling with cystic changes. If I could be sure it was a solid tumor I should be more in favor of its origin in the stomach wall—a leiomyosarcomatous type of tumor. Is that your experience, Dr. Schatzki?

DR. SCHATZKI: Yes.

DR. SOSMAN: You believe that we can rule out spleen, kidney and mesenteric cyst quite safely.

DR. SCHATZKI: Yes.

CLINICAL DIAGNOSIS

Omental cyst.

DR. SOSMAN'S DIAGNOSIS

Extramucosal tumor of wall of stomach—leiomyosarcoma or spindle-cell sarcoma?
Cystic tumor of tail of pancreas?

ANATOMICAL DIAGNOSIS

Neurogenic fibrosarcoma of stomach.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The preoperative diagnosis on the operative sheet was recorded as omental cyst. I suppose they meant mesenteric cyst. At operation a large cystic mass was found. It was adherent over a large area of the stomach and actually arose in the stomach wall. It was quite fluctuant and, when cut into, was found to be a necrotic tumor the central portion of which was liquefied and hemorrhagic. Microscopic examination shows a very undifferentiated, spindle-cell sarcoma. There were a few slightly enlarged lymph nodes on both sides of the stomach, which were resected along with the specimen. All of them were free from metastasis. However, these tumors almost never metastasize to lymph nodes; tumor cells travel via the blood stream to the liver. We thought that it was probably a fibrosarcoma rather than a leiomyosarcoma and that, because of the tendency to whorl formation, it was of neurogenic origin.

DR. SOSMAN: You say it definitely arose from the stomach?

DR. MALLORY: Yes; at no spot was there any ulceration of the mucosa. In many of these tumors a deep boring ulcer develops into the core of the tumor, but in this case the mucosa was intact.

DR. SOSMAN: Is there a fairly high degree of curability in tumors of this type?

DR. MALLORY: Yes.

DR. SOSMAN: Are they slow or late to metastasize?

DR. MALLORY: This one is quite malignant so far as they go. I should want to give a guarded prognosis but believe that the patient is probably cured.

DR. SOSMAN: Would you advise local post-operative x-ray treatment?

DR. MALLORY: We have little evidence that it does good in cases of spindle-cell sarcoma. I should not be enthusiastic about it.

CASE 29202

PRESENTATION OF CASE

A forty-nine-year-old housewife entered the hospital because of severe pain in the lower back and left leg.

Approximately one year before admission, without history of previous injury, the patient suddenly developed severe aching pain in the left sacroiliac area, which was relieved by an adhesive strapping and cleared after one week. Three and a half months prior to admission the pain recurred, being referred to the anterior aspect of the left thigh and

occasionally to the posterior aspect and calf. The pain was aggravated by coughing and sneezing and by movements of the lower spine. There had been no weakness, numbness, paresthesia or sphincter difficulty. Bed rest, adhesive strapping and leg traction, continued over a period of three months, gave no relief.

The family and past histories were noncontributory.

Physical examination disclosed a markedly obese woman who was obviously uncomfortable. The heart, lungs and abdomen were normal. There was no weakness of the legs. The ankle jerk was diminished on the left. Sensation was normal. Straight leg-raising was approximately normal on both sides and was not painful. There was no tenderness of the spine, sacroiliac region or legs.

The blood pressure was 140 systolic, 80 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 12.0 gm. and a white-cell count of 6900. The urine had a specific gravity of 1.010 and showed a + test for albumin; the sediment contained an occasional red cell, 25 white cells, a rare hyaline cast and 20 epithelial cells per high-power field. A blood Hinton test was negative.

An x-ray film of the spine showed considerable decalcification of all the visible bones. The lumbar spine showed slight scoliosis, with the convexity to the right. The first sacral segment was not fused, and there were marked degenerative changes about its articulations, the second sacral segment and the two iliums. There were also rather marked degenerative changes about the sacroiliac joints.

A spinal tap in the third lumbar interspace yielded xanthochromic fluid, which clotted on standing. There was no response to jugular compression, but a good response to cough. This fluid had a total protein of 2400 mg. per 100 cc. Colorless spinal fluid was recovered from the first lumbar interspace, and at this level there was a normal response to jugular compression and the fluid had a total protein of 294 mg. per 100 cc. A spinal-fluid Wassermann test was negative, and the gold-sol curve was 0001233411.

An operation was performed on the eleventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JAMES B. AYER: Can you say anything about the width of the spinal canal or erosion of the lateral masses?

DR. RICHARD SCHATZKI: Just glancing at these films I cannot see any more than the record states. There is no evidence of erosion. There is some osteoporosis and scoliosis, with slight degenerative changes.

DR. AYER: And a defect that is congenital?

DR. SCHATZKI: Yes.

DR. AYER: No evidence of erosion?

DR. SCHATZKI: No.

DR. AYER: Since there is no mention of cells in the spinal fluid, I assume that none were found.

One year before entry the patient's symptoms might reasonably be considered as having been due to sacroiliac or low-back ligament strain. With the advent of pain referred to the anterior thigh that had a sciatic distribution on the same side and was increased by coughing and sneezing, we are forced to consider a spinal or intraspinal rather than a peripheral cause for symptoms.

The demonstration of complete spinal-fluid block is proof that there was a space-filling mass or other lesions, such as meningeal adhesions, causing obliteration of the subarachnoid space; that this obstruction was focal—that is, between the first and the third lumbar vertebra—is indicated by the fact that dynamic studies showed a rise in spinal-fluid pressure on jugular compression at the upper level and on coughing at the lower. The fluid itself was abnormal at both levels, showing a difference in protein content quite characteristic of a noninflammatory focal lesion.

What type of lesion causes focal subarachnoid block and yet fails to cause symptoms that are characteristic of transverse section of the cauda equina?

Malignant tumors cause unilateral symptoms at first; by the time they produce subarachnoid block, the caudal canal is usually filled with cancer and the symptoms are bilateral. Epidural tumor and abscess likewise cause block only when compression from outside the dura is great, and the symptoms bilateral. In considering extradural lesions we must always think of a ruptured disk, but in my experience, block is caused only when the bulge is large and the symptoms are bilateral. Syphilis and tuberculosis give quite a different clinical picture, and the fluid of each contains appreciable numbers of cells.

Two types of tumor not infrequently cause unilateral symptoms, either pain or weakness, and yet are sufficiently large to obstruct fluid pathways—namely, neurofibromas of the nerve roots and dermoid or other congenital tumors originating in

the filum terminale. Either tumor may be associated with an anomaly of the spine, such as that demonstrated in this case. Of these two types the neurofibroma remains more focal, the congenital tumor usually filling and enlarging the canal. The latter usually becomes manifest in youth, whereas the nerve-root tumor may appear at any age.

My diagnosis is neurofibroma, involving a sensory root and lying between the first and the third lumbar vertebra on the left.

DR. HENRY R. VIETS: Although Dr. Ayer is too modest to mention it, it was he¹ who first pointed out that the spinal-fluid protein may be increased above a tumor as well as below it.

There is one other point of interest. Tumors growing from the nerve roots in the cauda equina, such as fibromas, are often somewhat mobile. On jugular compression the spinal fluid is forced down against the tumor and traction is exerted on the nerve root from which the tumor arises, thus causing pain in the area it supplies. This is a valuable test for localizing a tumor and for estimating its probable character, and was first described in 1928.² I do not know whether the test was carried out in this particular case. If it were positive, one would have expected that the tumor was a neurofibroma attached to a spinal root. The pain is a variation of that brought about by coughing, sneezing, yawning or straining at stool. The test, however, is not specific for neurofibromas attached to nerve roots, for it has been positive in patients with ruptured intervertebral disks.

DR. CHARLES S. KUBIK: Jugular compression caused severe pain in the back and in the anterior aspect of the thigh.

DR. W. JASON MIXTER: That sign also occurs in patients with ruptured disks.

DR. KUBIK: Dr. Mixter will tell us what he found at operation.

DR. MIXTER: A laminectomy was done, with fairly extensive exposure of the second and third laminae, which were removed, and the dura opened. Quite a large sausage-shaped tumor lay within the roots of the cauda equina. The roots were firmly adherent to the tumor and seemed to run through it. It was necessary to sever two fairly large roots in order to remove the growth. I could not make a definite diagnosis from the gross specimen, but I thought it was a neurofibroma.

CLINICAL DIAGNOSIS

Neurofibroma, region of second or third lumbar vertebra.

DR. AYER'S DIAGNOSIS

Neurofibroma, involving a sensory root and lying between the first and the third lumbar vertebra on left.

ANATOMICAL DIAGNOSIS

Neurofibroma, region of second or third lumbar vertebra.

DR. KUBIK: On histologic examination the tumor proved to be a neurofibroma.

The patient left the hospital about one month after operation, completely relieved of her pain. Since this type of tumor is benign and since the

tumor apparently was completely removed, the prognosis should be good.

Occasionally such tumors are multiple, occurring in other nerve roots or in peripheral nerves throughout the body and producing the clinical picture of neurofibromatosis or von Recklinghausen's disease. This patient, however, showed no evidence of the generalized form of the disease.

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CURRENT MILITARY AND CIVILIAN NEEDS FOR PHYSICIANS

PUBLISHED elsewhere in this issue of the *Journal* are statements by the surgeons general of the United States Army, Navy and Public Health Service and by the chairman of the Directing Board of the Procurement and Assignment Service concerning the current military and civilian needs for physicians.

It has recently been emphasized in these columns that more physicians must be dislocated and that the majority of these men must be obtained from urban areas. The official releases referred to above confirm these two statements, but they also imply

that the medical profession has been reluctant to make the necessary sacrifices. Such an implication is not altogether fair. Vast numbers of physicians of all ages have already volunteered for military or other governmental service, and as more are needed, they will be forthcoming. The medical profession of this country has never failed to assume its responsibilities, and it will not do so now!

PSYCHOTHERAPY

"It has been a profound shock to me on several occasions that the patient preferred to change his doctor rather than his life-style," writes Dr. Charles Hubble in a very readable article, "Charles Darwin and Psychotherapy," in the February 13 issue of the *Lancet*. Dr. Hubble does not mean that he is still being shocked in 1943 but refers to his adolescent days in psychotherapy. The quotation brings to mind such wisdom as is contained in the adage "Let well enough alone"—a way of saying that although a situation might ideally be better it probably would be worse if tampered with. "Let sleeping dogs lie" is another form of admonition in the same general direction, as is James Thurber's advice to "let your mind alone."

In an analysis of Charles Darwin's chronic, almost lifelong, neurotic illness, Dr. Hubble suggests that had the great naturalist been subjected to strenuous psychotherapy of the twentieth-century variety, *Origin of Species* might never have been written. The zealous psychotherapist would have attacked Darwin's neurotic manifestations, would have jostled them about a bit and, unless wise, would have broken down the protective fence behind which Darwin accomplished his great scientific work—all of which emphasizes the fact that, in spite of the awe-inspiring changes produced by science, the psychotherapist should keep in mind the steadying conception of the limits of human modifiability.

Sometimes it is said that psychotherapy should not rest content with the removal of a symptom; it should go on to discovery and elucidation of the underlying cause. On the contrary it might

be said, if one pays due attention to Dr. Hubble's admonition concerning "sleeping dogs," that psychotherapy should not attempt to remove symptoms in some people, except on a level of light reassurance. What is attempted should depend on what is asked for. Darwin did not want to be cured. He asked, in effect, to be reassured that he was sick and needed treatment, but not cure. If he had been cured he would have had to give precious time and energy to innumerable strength-sapping interruptions.

For a man who accomplished so much, Darwin's daily schedule was unusual. He worked only four hours and during the remainder of the time rested on a sofa or took it easy in one way or another. If he attempted anything outside his established routine he suffered with excitement or a stomach upset. His nights were generally poor, since often he could not stop the activity of his mind. But the resting and bad nights did not amount to so many wasted hours. It was during those hours that Darwin contemplated and nourished the ideas that developed into superior attainment. He did what Harvey Cushing once advised—took time for contemplation so that ideas might be properly fertilized.

Dr. Hubble interprets Darwin's chronic illness as an unconscious means of husbanding energy for his work. One with a direct, honest approach to life might ask why Darwin needed to use subterfuge, unconscious or conscious. Why did he not frankly state that he required so much time for his work and that he had neither the inclination nor the energy for occupations that seemed to him noncontributory? The answer to this, thinks Dr. Hubble, lay in Darwin's great kindness and sensibility. It would have taken a ruthlessness and unrefined selfishness, of which Darwin was not capable, to say forthright to family, friends and professional associates that he did not have time to give them.

Whether or not the interpretation of Darwin's illness is valid, the sanguine psychotherapist should remember that what is looked on as being neurotic

illness is sometimes the best adjustment that can be made by the particular person. Most people with neurotic troubles are not geniuses conserving their strength, but some of them have made certain peculiar adjustments because of biologic necessity and not because of a blind stumbling into disease.

If people could honestly and openly accept, and if their environments would permit them to accept, their limitations, there would be less psychologic impulsion toward neurotic development, but such acceptance requires a hardness or an ingenuousness not frequently found. Ingenuousness is a childlike quality, and the maturing process in a world of material values does not nurture it. Also, a part, the ambitious part, of the person's very nature may destroy it.

Some people jump, not through hoops, but when startled. The threshold for visceroautonomic reactions may depend on innate, constitutional or hereditary determinants as well as on the influence of environment and circumstance. Instability of psychosomatic reflexes does not necessarily indicate a psychogenic origin for the instability. Dr. Hubble rightly considers this possibility in his analysis of Darwin's "illness."

Because headaches have no clearly defined or discovered physical cause does not warrant the assumption that they are due to psychogenic factors. A sincere but too ardent therapist might add to his patient's suffering by insisting that he rout by self-searching introspection the cause of his disease, when it never could be routed by such a method since it lies in the biologic and physiologic warp and woof of the personality.

The truth may make us free; however, not knowing what is ultimate truth, physicians should be a little cautious in thrusting their own brand of it down patients' psychosomatic throats.

MEDICAL EPONYM

VOLKMANN'S CONTRACTURE

This was first described in 1869 by Professor Richard Volkmann (1830-1889), of Halle, in his section of Pitha and Billroth's *Handbuch der allge-*

forces may develop that will destroy the practice of medicine as we know it. This would be disastrous and it is something that we cannot afford to allow to come about. In all seriousness, the doctors of medicine in the United States should take stock carefully of their own immediate situations and should give every assistance in planning to see that medicine plays its responsible part in this and coming years.

STATEMENT OF THE SURGEON GENERAL OF THE UNITED STATES PUBLIC HEALTH SERVICE

During the next twelve months, the United States Public Health Service will require approximately 600 medical officers for full-time active duty in the reserve commissioned corps. These physicians will be recruited on an average of 50 a month—25 for service in the United States Coast Guard, and 25 for general service.

In addition to the medical officers assigned to the Coast Guard, physicians are needed for duty in the marine hospitals and the medical program of the War Shipping Administration, as well as for detail to general public-health work in state and local health departments, and for such specialized war programs of the Public Health Service as tuberculosis control, venereal-disease control, industrial hygiene and community medical services.

The Public Health Service also expects this year to commission some 5000 physicians in the inactive reserve. These doctors will be available for active duty in the event of acute emergency in their own or nearby communities. They will not be called for active duty unless an acute emergency exists, and will be retained only for the duration of such an emergency. This recruitment of inactive officers is undertaken as a part of the co-operative program of the Public Health Service and the Office of Civilian Defense.

The needs of state and local health departments for physicians have increased greatly during the past year. In January, 1942, it was estimated that state and local health departments would need 600 physicians. As of January, 1943, the exact needs have not been determined, but the Public Health Service has, at the present time, requests from the states for 185 medical officers to be assigned to duty in war areas alone.

According to reports from state chairmen of the Procurement and Assignment Service, as of March 23, 1943, 286 additional doctors for civilian practice are needed in one hundred and seventy-six counties located in thirty-eight states. Another twenty-two counties in the same states reported a shortage of physicians but did not specify the numbers needed. In the remaining ten states, no needs were reported. These one hundred and ninety-eight counties reporting immediate needs represent only 7 per cent of the two thousand, six hundred and fifty-four counties in the thirty-eight states, and only 6 per cent of all counties in the country. Nevertheless, it is apparent that civilian communities are feeling the pinch of the shortage of physicians increasingly, since experience has shown that local needs become acute before they are expressed in formal reports.

In the joint studies made in forty-two areas by the Public Health Service and the Procurement and Assignment Service, it has been determined that 59 physicians and 5 dentists, or 64 medical and dental personnel, are needed in these areas—an average of 1.5 per study. The Public Health Service has been requested to supply 13 of

these physicians and dentists, or 23 per cent of the determined need. On the basis of these forty-two studies, it is estimated that 500 physicians and dentists will be needed in three hundred and thirty-two areas to be surveyed in the next coming fourteen months, or by June 1, 1944. It is anticipated that 80 per cent of these, or 400, will be supplied by voluntary relocation through the regular channels of the Procurement and Assignment Service, and that the Public Health Service will be requested to assist in meeting the needs for the remaining 20 per cent, or 100 physicians and dentists. This may be done either through financial assistance to physicians desiring to relocate in areas requiring their services, or through assignment of Public Health Service personnel on request of the proper authorities.

Although it is impossible to project with accuracy the 1943 needs of civilian communities, we must face the fact that the shortage undoubtedly will increase during and after the filling of the 1943 military quotas; and that the chances of meeting civilian needs as well as replacing physicians who die or withdraw from practice because of disability will correspondingly decrease. Furthermore, we cannot predict at this time the possible needs of certain rural areas which now may be adequately supplied but which will require additional public health and medical services during 1943 should the Government move a large number of farm families into these areas for the food-production drive. It is believed that joint action of the Public Health Service and the Procurement and Assignment Service will serve to meet urgent needs in civilian communities.

STATEMENT OF THE CHAIRMAN OF THE DIRECTING BOARD OF THE PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS AND VETERINARIANS

Figures are now complete on the 1942 quotas for supplying physicians of the various states. Forty states have exceeded their quotas. Five states were above 90 per cent of their quotas. Four states—New York, Connecticut, Massachusetts and Nevada—were below 90 per cent of their quotas.

Nevada is the lowest state, but has a total quota of but 35 doctors. It has provided 23 and deserves special consideration because its population is thinly scattered over wide areas.

This statement would not imply any reflection on the patriotism of those members of the medical profession who have been marked available by the Procurement and Assignment Service in the other three states and who have not sought a commission. I would only present the facts and let each one draw from these facts whatever deductions he individually chooses.

Certain unavoidable considerations must be faced in these figures. Four states failed to provide 90 per cent of their 1942 quotas of doctors for the services. Three of these states—New York, Connecticut and Massachusetts—are eastern seaboard states and among the most populous ones in the Union. These populous states have large cities in them which now have more doctors per thousand persons than most other parts of the country. Largely because those doctors marked available by the Procurement and Assignment Service have not sought commissions these states are below their quotas.

Unless more of the doctors found available for military service by the Procurement and Assignment Service in

these cities apply for commissions in the armed forces with reasonable promptness still more doctors must come from rural communities. This will greatly complicate the problem for those communities in their own and other states since many rural communities are already none too well supplied with doctors. Such inequalities in medical service now exist are in a considerable measure the result of the conditions herein stated and cause occasional problems of rural medical care which become practically insurmountable for the Procurement and Assignment Service with its present limited authority. With all these facts in mind, with the responsibility of medicine to the country and to itself such as it is, the quota figures particularly in New York, Connecticut and Massachusetts should be brought up to par by an intensive effort of the state medical societies through their executive bodies preferably by an organized state medical society campaign.

The provision of doctors for the armed forces is not only the special obligation of medicine but a responsibility which it acknowledges and accepts as its part in the war effort. Each state that has not met its 1942 quota will be apt informed of its position in relation to its quota and its position in relation to other states. Otherwise a state's denied pardonable pride of satisfaction in meeting its quota or pampered against facing a distasteful position in relation to other states.

MISCELLANY

PLEUROTOMY IN THE TREATMENT OF ACUTE MINIMAL TUBERCULOSIS

The intensification of early diagnosis campaigns and the widespread use of mass x raying in war industry and armed service can result only in the discovery of more and more tuberculosis among the apparently healthy. It is obvious that a large proportion of these cases will be preclinical in the old meaning of the term. Today we must modify our terminology to acknowledge that tuberculosis found early deserves and demands early treatment. Finding the disease in a stage devoid of symptoms imposes on us the obligation so to appraise cases and so to select treatment that development of symptoms will not occur and spread of tuberculosis will be prevented. A recent article emphasizing this point (Korb, E. G. Pleurothorax in the treatment of acute minimal tuberculosis *California & West Med Tuberculosis Supplement*, July, 1942) is abstracted below.

* * *

In its most characteristic connotation, the term acute minimal tuberculosis implies a recent or relatively recent small area of pulmonary infiltration without cavitation. This lesion is most often found beneath the clavicle or in the first or second anterior interspace and is described by the roentgenologist as soft.

Typically, we might expect the patient to be a healthy appearing adolescent or young adult who has been in direct contact with a case of active tuberculosis. Cough, sputum, hemoptysis or other classic symptoms have usually not appeared. Constitutional symptoms are absent or are limited to malaise, anorexia or slight weight loss. Careful physical examination of the chest is usually negative. The Mantoux test is positive whereas the sputum or gastric contents may or may not be positive.

Although the foregoing might be described as

each individual case represents a problem for the physician to solve, not only on the basis of his experience in the usual methods of treatment but also on his knowledge of the social background, economic status and psychology make up of his patient. Such important considerations as age, sex, race, occupation, co-existing diseases and length of exposure to tuberculosis must be carefully weighed.

To obtain this information a period of observation at home conditions that is absolute bed rest is essential. Whenever possible this period should be spent in a hospital for the tuberculous away from the distracting influences of the family. This period should be measured in terms of weeks rather than months.

Occasionally a lesion that roentgenologically seems entirely typical will clear in the space of two or three weeks, indicating a mistaken diagnosis.

The acute early infiltrate is always an unstable lesion. It soon regresses or progresses. Absorption or fibrosis may follow or there may be rapid or slow progression with caseation, liquefaction and excavation.

The indications for pleurothorax are numerous but in the opinion of the author the following are the most important. The production of positive sputum indicates that tissue necrosis has already occurred and for this reason such cases should be given pleurothorax promptly. Likewise lesions with x ray evidence of beginning breakdown should be collapsed immediately.

If the lesion continues to progress on bed rest immediate collapse is indicated even though the sputum remains negative. In addition to serial x ray films, careful pulse, temperature and respiration records, the sedimentation index and a differential white-cell count are valuable indices of the patient's course under therapy.

There are supplementary, more personal indications for pleurothorax which have not been mentioned so prominently in the literature. The family wage earner may prefer immediate collapse and the attendant shorter period of hospitalization and disability to the more conservative if equally effective period of absolute bed rest.

Likewise the nonoperative, the unintelligent or the trouble-making patient may be much better controlled by pleurothorax. In the experience of the author the most difficult patient to handle in the sanatorium is the apparently healthy individual with no symptoms. He finds it boring to maintain himself at bed rest and all too frequently leaves the hospital against medical advice. Many times pleurothorax has been instituted because it seemed the only way to control both the patient and his lesion.

The adolescent girl with minimal tuberculosis requires especially close observation and if there is any question concerning lack of satisfactory progress pleurothorax should be done.

Others have listed as advantages of pleurothorax in these cases the shorter period of hospitalization and disability, the shorter conversion time in case the sputum is positive and the fact that in their opinion the end results are better. It should also be emphasized that the physician sees his pleurothorax cases oftener and any change will be detected sooner. He is likewise in a better position to regulate their social and vocational activities.

The chief arguments against pleurothorax are the inconvenience to the patient and the long and expensive period of

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portant, the danger of complications. Although the latter are rare in minimal cases, pleural effusions, empyema, spontaneous pneumothorax, bronchopleural fistula and nonexpansile lung do occur.

Summary. There is no such thing as a "routine" treatment for minimal tuberculosis. It is equally absurd to say that every case should receive pneumothorax as it is to say that collapse should never be used until the disease becomes moderately or far advanced.

Beginning tissue necrosis, positive sputum and lesions that are progressive on absolute bed rest are, in the opinion of the author, absolute indications for pneumothorax.

Once a small area of pulmonary infiltration has been definitely diagnosed as being tuberculous, the patient should be treated for *tuberculosis*; and not for a "spot on the lung." There are too many patients with "spots on the lung" who only discover that they have tuberculosis when referred to a specialist after their disease has progressed beyond the minimal stage.

If the early-diagnosis campaign is justified, as it most assuredly is, then an early-and-adequate-treatment campaign is likewise indicated.

The adequate treatment of acute minimal tuberculosis does not consist in merely telling the patient to "take it easy." It demands a period of absolute inactivity supplemented by pneumothorax or other collapse procedures as deemed advisable by the attending physician.—Reprinted, in part, from *Tuberculosis Abstracts* (May, 1943).

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MARCH, 1943

DISEASES	MARCH 1943	MARCH 1942	SEVEN YEAR MEDIAN
Anterior poliomyelitis	3	0	0
Chicken pox	1601	1793	1471
Diphtheria	10	16	14
Dog bite	717	841	754
Dysentery, bacillary	5	0	3
German measles	8210	1182	105
Gonorrhea	327	323	384
Measles	6419	3245	3245
Meningitis, meningococcal	130	24	10
Meningitis, other forms	11	27	*
Mumps	1077	2791	1303
Paratyphoid fever	2	0	3
Pneumonia, lobar	372	516	654
Scarlet fever	2501	1457	1184
Syphilis	479	443	492
Tuberculosis, pulmonary	313	262	285
Tuberculosis, other forms	20	13	28
Typhoid fever	0	2	3
Undulant fever	2	2	4
Whooping cough	875	1004	969

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from: Norfolk 1; total, 1.

Anterior poliomyelitis was reported from: Amherst, 1; Boston, 1; Everett, 1; total, 3.

Diphtheria was reported from: Cambridge, 1; Camp Myles Standish, 2; East Brookfield, 1; Grafton, 2; Lowell, 1; Stoneham, 1; Tewksbury, 1; Wakefield, 1; total, 10.

Dysentery, bacillary, was reported from: Boston, 3; Winthrop, 1; Worcester, 1; total, 5.

Encephalitis, infectious, was reported from: Brockton, 1; Newton, 1; Salem, 1; total, 3.

Lymphocytic choriomeningitis was reported from: Fort Banks, 1; total, 1.

Malaria was reported from: Camp Edwards, 1; total, 1.

Meningitis, meningococcal, was reported from: Attleboro, 1; Barnstable, 2; Bedford, 1; Belmont, 1; Boston, 19;

Brockton, 1; Cambridge, 5; Camp Edwards, 32; Canton, 1; Chelsea Naval Hospital, 1; Dartmouth, 1; Easthampton, 1; Easton, 1; Everett, 2; Fall River, 2; Falmouth, 1; Fitchburg, 2; Fort Banks, 4; Fort Devens, 3; Framingham, 1; Greenfield, 2; Hingham, 1; Kingston, 1; Lowell, 4; Malden, 2; Medford, 1; Melrose, 1; Middleboro, 1; Millbury, 1; Needham, 1; Newton, 1; North Reading, 1; Norwood, 1; Plymouth, 2; Quincy, 2; Rockland, 1; Salem, 2; Sharon, 1; Shrewsbury, 1; Somerville, 3; South Hadley, 1; Springfield, 1; Stoughton, 1; Swampscott, 2; Townsend, 1; Watertown, 1; Wellesley, 1; Westover Field, 2; Weymouth, 1; Winchester, 1; Worcester, 6; total, 130.

Meningitis, other forms, was reported from: Boston, 6; Brockton, 1; Cambridge, 1; Lynn, 1; Woburn, 1; Worcester, 1; total, 11.

Paratyphoid fever was reported from: Braintree, 1; Cambridge, 1; total, 2.

Septic sore throat was reported from: Amesbury, 1; Boston, 9; Cambridge, 3; Camp Edwards, 1; Ipswich, 1; Medford, 2; Merrimac, 1; New Bedford, 5; Newton, 1; Wakefield, 2; Westford, 1; total, 27.

Trachoma was reported from: Boston, 2; total, 2.

Undulant fever was reported from: Conway, 1; Greenfield, 1; total, 2.

Meningococcal meningitis continued on the increase during March, reaching the highest figure on the records. Scarlet fever, too, was more prevalent than at any time since 1906, with the exception of March, 1927. Measles and German measles continued at an unusually high level.

The following diseases in addition to the above exceeded their respective seven-year medians: anterior poliomyelitis, chicken pox, bacillary dysentery and tuberculosis (pulmonary).

Under the seven-year median were: diphtheria, dog bite, gonorrhea, mumps, paratyphoid fever, lobar pneumonia, syphilis, tuberculosis (other forms), undulant fever and whooping cough.

Typhoid fever in March repeated the January record of no cases reported. These two months have set up an all-time record.

NOTES

Dr. Charles F. Wilinsky, chief medical officer of the Boston Committee on Public Safety and director of the Beth Israel Hospital, was recently awarded the medal that the Boston City Club presents annually to the resident of Boston, not holding an elective position, who has performed the most meritorious service for the welfare of Bostonians during the year in question. The basis of the award was Dr. Wilinsky's work in organizing the medical section of Boston's civilian-defense effort, as well as his personal services and those of his medical organization during the Cocoanut Grove disaster.

Dr. Douglas A. Thom, director of the Habit Clinic for Child Guidance, Boston, has been granted a leave of absence and is on active duty with the Medical Corps of the Army of the United States, as neuropsychiatric consultant to the Second Service Command, with the rank of lieutenant colonel. Dr. Harvey Spencer, psychiatrist on the staff of the Judge Baker Guidance Center, has been appointed acting director of the clinic.

(Notices on page xiii)

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SMALL PUDDLES*

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HOLYOKE, MASSACHUSETTS

THE first problem to confront a fledgling physician is the choice of habitat, or the arena in which theories are to be put to the test, the sphere that he hopes to influence, or, if you prefer your metaphors mixed, the waters on which the enriched bread of his services shall be cast. In wartime such a discussion might seem to be entirely without point, since all graduates of approved medical schools march directly into service uniforms with little or no choice as to settlement. And in a planned economy, even in the absence of war, of course the individual concerned is the last person to be consulted about such details.

Nevertheless, I choose to continue in this unpromising vein in the hope that we may salvage perhaps some historic value from a nostalgic review of the procedures of a simpler day. At least the effort is no more out of place than is a so-called "orator" who has been thrust without consultation from the dead-end silence of the vice-presidency to the uproar of this loud-spoken rostrum.

In the choice of field of practice, if the matter has not already been settled by some such accident as birth, the question of prime consideration is size—whether the community shall be large or small, whether provincial or metropolitan. Thirty years of service in an outlying district have prepared me to speak to some purpose from the pre-terurban, if not bucolic, point of view. Though this may be conceded, the intrusion of the personal touch, which I trust will be overlooked, necessitates a separate apology. I can speak with authority only of my own experience, but *ipso facto* the topic, "Small Puddles," I hasten to add, holds no pediatric connotation.

Fortunately, our own society has prepared statistics "as of February 15, 1942," which are appended to the *Directory of the Officers and Fel-*

lows. Offhand the conclusion seems justified that the Secretary should assume the responsibility for the accuracy of these figures. Thus I would involve in their defense our able incumbent, Michael A. Tighe, whose gestures and aptitude for debate are beyond question more convincing than mine. Inasmuch as the current figures show in most instances an increase over the recapitulation of 1940, it is clear that war service had not yet depleted the ranks of membership and that the figures therefore are a reliable reflection of pre-war conditions.

The Commonwealth of Massachusetts has been divided medically into eighteen districts, all but six of which are crowded into the eastern third of the state, where, as is obvious, the bulk of population dwells. Of 5074, the total number of active, resident fellows of the Massachusetts Medical Society as of the above date, 661 claimed Suffolk as their district. Norfolk sheltered 862, while the number in Middlesex South was 1005. That is to say, practically half the membership was enrolled in three districts alone, swimming either in or within easy jumping distance of the major puddle, Boston. There can be little question therefore that a great many incipient practitioners have preferred to risk the anonymity of being just another frog in a large and crowded puddle. This observation is further verified by the 2.4 per cent increase in Middlesex South during the past two years, which is more than twice that of Hampden (1.1 per cent) and almost twice as much as Norfolk's (1.6 per cent). The large Worcester puddle increased even more, 4.4 per cent, which should discourage further additions. The remarkable increase of 14.7 per cent in Barnstable may easily be explained by the establishment of Camp Edwards on the Cape. At any rate, there would seem to be no further room there for expansion. Of necessity, then, at least half the new men must look for placement in the small

*The Annual Oration, delivered at the annual meeting of the Massachusetts Medical Society, Boston, May 25, 1943.
†President of staff, Holyoke Hospital

puddles. The heaviest agglutination of frogs was found to be as follows:

Middlesex South	1005
Norfolk	862
Suffolk	661
Worcester	425
Hampden	341
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Total	3294

This merely substantiates the well-known fact that metropolitan centers seem to exert a strong attraction for numbers of individuals in all walks of life, including the bypaths of medicine. Some of them doubtless take comfort in the presence of a multitude of neighbors. The big city offers a challenge to others, particularly those who have been reared in less sophisticated centers. Small-town boys—and girls—have always seemed to like to prove that they can make good in the major leagues.

Still others find themselves metropolitans by accident. Paul White is one of the group which can qualify by the accident of birth. He was born in one of Boston's suburbs to grace the maturity of an honorable and capable practitioner of medicine whom it was my privilege to visit as a medical student. Only recently we have learned through a pleasing stroke of notoriety by what a narrow margin he avoided the tragic accident of serving a life term in the Tower of London instead of in the Bulfinch Building with such credit.¹ If Cornelia Skinner's mother had been less gifted, her daughter's smuggled measles might have altered history, even though they did not permanently change the damsel in distress.

I am at a loss, however, to explain the decision of a lovable Al Hornor who transplanted his sunny smile out of the Deep South into the bleak Back Bay so successfully that his happy accent is still unimpaired after thirty years of exposure to the harsh east wind that sweeps up Boston Harbor. I believe it was clinched by the power of the scientific spirit that impelled him to continue the pursuit of knowledge at the fountainhead. No man may question this, the best of reasons for settling in a puddle that seemed to be overcrowded. In the waters of science there is always room for talent and for devotion.

But I have seen, and so have you, not a few truly pathetic figures haunting the purlieus of the large metropolitan hospitals in the vain hope of a recognition that cannot come to all. Many of these misguided creatures could have been happy and respected frogs if they had shifted to smaller puddles before it was too late, or, better, had chosen wisely in the first place.

The accident of medical heritage no doubt is a factor in deciding many settlements, but no more so in rural than in urban localities. Nor is there always assurance that a medical son will elect to enter practice with his father. Not seldom he has preferred to strike out for himself, though the majority of such associations seem to be mutually appreciated. I have discovered that this factor has influenced 15 per cent of the fellow-occupants of our local puddle. Perhaps this is a fair average figure for all communities, but I have no available evidence to prove it either way. It is of interest rather than significance worthy of further consideration.

The less frequented waters in remoter regions of the Commonwealth were chosen in descending sequence thus:

Berkshire	134
Worcester North	102
Bristol North	75
Hampshire	73
Barnstable	61
Franklin	48
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Total	493

It is somewhat startling to realize that all the frogs that inhabit the five least populous districts outnumber the total in the Hampden district by only 18 and that Hampden, in turn, stands only fifth in density of frog-units. Here, then, should be found *Lebensraum*, or better, room to swim in peace.

Passing from general considerations to particulars, or from ponds, let us say, to the study of the puddles in question, the Worcester district leads in number with forty-three, eleven of which are unoccupied by frogs. At the other extreme stands Suffolk, with only seven puddles and not one cipher among them. For contrast, the extremes in both occupied and unoccupied puddles have been grouped as follows:

NUMBER OF PUDDLES

MOST		LEAST	
Worcester	43	Middlesex South ..	13
Norfolk	36	Franklin	13
Plymouth	32	Middlesex East ..	12
Barnstable	30	Bristol North ..	7
Essex South	24	Suffolk	7

EMPTY PUDDLES

MOST		LEAST	
Berkshire	21	Essex North	1
Franklin	17	Essex South	1
Hampshire	12	Middlesex East ..	1
Worcester	11	Norfolk South ..	0
Hampden	9	Suffolk	0

It would appear that the Berkshire, Franklin and Hampshire districts offer more open expanses

of frogless water than all others, the westernmost district in particular, for in Berkshire, the empties outnumber the encumbered puddles by twenty-one to sixteen. Nor should Worcester be overlooked, with eleven vacancies. At least that was the picture in 1942. The fact should be borne in mind for future discounting, that there has been a large industrial expansion in various parts of the State that may vitiate these findings. Only the future will provide the answers to such questions as to how much of the war work can be salvaged, and whether or not physicians will be drafted where they are needed without the privilege of choice.

It might be kind, before the rush of nineteen-forty-niners sets in for the gold-bearing hills, to point out the unvarnished truth about these ghost-town puddles. With a barrier of ice and snow such as has but recently melted, the hill towns can challenge the most rugged individuals and put them to the test. Some few frogs before this have given up the fight, as others doubtless will in due time, because they could not sustain themselves and their families under such conditions. What is more to the point, they could not subsist on scenery alone.

But for some years now young men have not felt that they were called on to bury themselves, as the quaint phrase put it, when practice in the country was proposed. A. Warren Stearns, as dean of Tufts College Medical School, was one of the first to do something practical about stemming the tidal wave of specialism that had dangerously thinned the ranks of family doctors in the less populated districts. The scholarships that he was instrumental in raising still make it possible to nullify the prediction that Richard Cabot uttered with such finality a quarter of a century ago, that the general practitioner of medicine would soon be entirely extinct.

"As I go into towns like Bedford," he wrote in answer to my query, "which had not had a doctor for many years, and find the place that Dr. Lord has made for himself, I feel happily justified in what we have tried to do. And so I might go on, with Dr. Cole in Westford and Dr. Lewis in Groton, perhaps multiplying these several hundred times." "The people speak gratefully to me," he added, "for what we have done for the towns."

The towns, in fact, are no longer isolated as a result of modern contacts, tangible or air borne. And even tangibles promise to become air borne when a helicopter shall transport each practitioner, or television shall bring the image of the patient's ailing tongue with no expenditure of effort at all. There should be ample opportunity in those

halcyon days ahead to enjoy the sunsets behind Mount Wachusett or a ski run to the summit of Greylock between calls.

As a matter of fact, there has always been time for frogs with receptive eyes to observe for themselves the manifestations of nature no matter where they are stationed. Even Roger Babson, the urbanite, has made a business of collecting sunsets. One of his choicest was observed from a hotel window in the heart of New York City. Again, I am sure that you too would have been thrilled, as I was, at the sight of that handsome but elusive duck, the redhead, taking refuge with a group of mallards in a wintry puddle in the Fenway within a stone's throw of Brookline Village. At least there could be no doubt of the reaction enjoyed by a fellow-practitioner when I pointed out for him the snowy crest of a great American egret across the back water of the Ox-Bow on our Connecticut River not so long ago. He had traversed the length of the State, but the heron had flown the long miles north from the Everglades of Florida.

And human nature, the never-ending source of wonderment and study, is universally available, in puddles large or small. Geographical considerations are not paramount in such studies, nor, in fact, in the full enjoyment of life when viewed with understanding. Lin Yutang,² for example, maintains that the West still has much to learn from China in such matters. "What the modern world needs," he wrote, "is not more intellectual brilliance, but more life wisdom." Not without point he added, "The truest test of a civilization is not how you are able to conquer and to kill, but how you can get the greatest kick out of life."

From a small puddle it is but a question of minutes rather than hours to get down to earth for a profitable communion with nature, whether in pursuit of birds or biddies, as individual taste may dictate. In like manner the greater intimacy of the smaller community brings human beings more readily within range. They are not so apt to remain lay figures to be laid aside at the close of day, or the records of their troubles merely to be filed with other interesting data at the end of the service. There indeed is the rub. They have feelings that must be respected—and the spotlight of publicity searches out every action of the upstart in their midst.

Conversely, when knotty problems have been solved, and the perishing have been rescued—the appreciation is prompt and lasting. The resulting relation of affectionate trust and respect outweighs many times the larger financial rewards that are said to accrue in the more ambitious puddles. After thirty years of such experience, I can

underline this last as the most convincing argument in favor of practice in small puddles.

It is more feasible, likewise, to share the public life of a small community. Such participation, though, may prove to be a liability. Indeed, a backward glance over the history of the particular puddle that I call home reveals the downfall of several frogs who played at politics. These catastrophes merely serve to re-emphasize the truth of the assertion that Medicine is a jealous mistress, and intolerant of rivals. A physician, I believe, even in a small town, should not limit his usefulness by taking sides except in matters of principle. There are too many caesars already without us to tend to such affairs. Nevertheless, it is still true that a willing frog may serve to good purpose by taking his share in the life of all who inhabit his own small puddle. During a lifetime spent in such surroundings, unknown talents may be discovered that never would have seen the light of day, and opportunities will multiply to study uncharted problems.

Jenner, for one, often has been held up as an example of what an alert mind can accomplish in a small community. Horace Wells, of Hartford, is another, and Austin Flint, of Northampton and Buffalo. Then there is Rafinesque of Kentucky, who anticipated Darwin's observations on deviations and mutations by twenty years. For a change, let me cite the case of Karl, the son of Nils, of oldtime Sweden.³ He hewed for himself the Latin surname of Linnaeus out of his family's linden tree and won fame for the name by patiently classifying the number of stamens and pistils of flowers that bloom in the spring, while medieval herbalists still floundered. But when it

came to taking a wife, the country boy returned to his small puddle for thrifty Sara Moroca, who is said to have thrashed her daughter, spoiled her son and urged her husband to quit meddling with science and turn to earning fat fees as a physician at the Court of Gustavus the Third.

But what of "ziss frog," as Franz Pfaff used to say, the one whose motives should be most familiar? Once he had to choose like other beginners between a mighty puddle and a small one. Continued research in bacteriology with A. I. Kendall was worthy of most serious consideration. And the academic life with regulated hours held a strong appeal. Yet the lure of a vast metropolis was more easily denied. Anticipation of new scenes soon faded under the potent charms of one small puddle that lay within the broad curve of the "Long River" and mirrored the form of the familiar mountain. Prospective pursuit of fractious anaerobes yielded to the call of native flora and fauna. In other words, the tap roots and family ties proved too strong to be torn loose. So one more decision must be credited to natal implantation.

Hear ye, then — ye who are about to enter upon the practice of medicine. Do not abandon hope, but elect instead to agitate some small puddle just as this stiff-jointed frog chose to do. It is certain that he would do so again if the choice, by some magic of Merlin, ever should recur.

207 Elm Street

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PRACTICAL CONSIDERATIONS IN THE THERAPEUTIC USE OF BLOOD DERIVATIVES*

COMMANDER L. R. NEWHOUSER (MC), U.S.N., AND LIEUTENANT E. L. LOZNER (MC), U.S.N.R.

BETHESDA, MARYLAND

WITH the increasing availability and use of liquid, frozen and dried human citrated plasma and of human serum albumin has come the realization that these blood derivatives are frequently not merely substitutes for whole blood but therapeutic agents in their own right, each with its own indications and contraindications and each presenting its own practical problems. In order to prevent the misuse of any of these derivatives and their consequent discredit, it is thought desirable to review certain of these practical considerations.

SERUM ALBUMIN

The most recent of these blood derivatives—namely human serum albumin—perhaps deserves the first attention, because certain misconceptions concerning its use have already arisen. Albumin should not be considered a substitute for plasma, and certainly not for whole blood. It represents a relatively stable concentrated solution of that fraction of the plasma proteins mainly responsible for the maintenance of the colloid osmotic pressure of the blood, and its chief advantages exist where storage or transportation space is at a premium. Thus, it may be of value in some military situations. However, in medical establishments of moderate size, ashore or afloat, where space is available for the storage of dried plasma, there are few, if any, indications for the use of serum albumin. Human serum albumin, therefore, will not be made available for routine use in such installations.

The chief dangers in the use of human serum albumin arise from the facts that it represents but one of the serum proteins, and that it is extremely hypertonic and supplies practically none of the fluid that may be needed in the treatment of traumatic shock, burns or hemorrhage. Woodruff and Gibson¹ have already reported the case of a burned patient treated with albumin to a point where the albumin-globulin ratio went to 67:0.7 and the prothrombin time was prolonged. Inasmuch as complement and antibodies are also

contained within the globulin fraction, it is evident that this sort of situation is fraught with dangerous possibilities. In burns, citrated plasma should follow albumin as soon as possible, arrangements should be made to transport patient promptly to an area where this is feasible or to transport plasma to the patient.

In traumatic shock, albumin must be considered solely as an emergency first-aid measure. Precautions (included in every package of se albumin) outlined by the Committee on Clinical Evaluation of Human Albumin, relative to increasing hemorrhage, to aggravating existing hydration, to increasing apparent anemia, to potential pulmonary edema, to the limit of dilution and to the stability of the solution, must be kept constantly in mind.

If it is desired to administer a hypertonic derivative, as for example in hypoproteinemia in certain burned patients, concentrated plasma may be preferable to albumin. The former may be administered very simply with the standard Army-Navy package of dried plasma, as described below.

The concentrated solution of human serum albumin is quite stable at the moderate temperatures encountered in the temperate zone. The package, however, must not be kept at freezing temperatures or at temperatures exceeding 50°C. (122°F). At temperatures approaching the latter level, denaturation and gel formation may take place, and long storage at ordinary temperatures a small amount of fine flocculation has occasionally been observed. So long as these reactions are not excessive, they do not affect the efficacy or stability of the product. However, as a precaution measure should excessive flocculation occur, a fine filter has now been included in the standard Army-Navy package of normal human serum albumin (concentrated).

LIQUID PLASMA

It is quite evident, from the experience acquired to date, that plasma, when prepared by the closed method with scrupulously aseptic technique, may be preserved in the liquid state at room temperature in a medical establishment in the temperate zone for at least as long as fourteen months. Over two thousand administrations of

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prepared and preserved in this manner by the Plasma Department of the Naval Medical School have been analyzed, with a reaction rate of approximately 1 per cent. The permissible temperature range of preservation probably lies between 15 and 30° C. (59 and 86° F.). Below this range excessive fibrin precipitation may occur, and above this range protein denaturation occurs rapidly. Although a small amount of fibrin precipitation is almost inevitable when plasma is preserved in the liquid state, this does not affect its efficacy or safety. It is imperative, however, that a filter be used in the intravenous set when the plasma is administered. Numerous types of filters have been devised for this purpose, and most of them are satisfactory. Glass cloth and stainless steel mesh, alone or in combination with glass beads or latex airfoam, when properly prepared and assembled, have been used successfully at the National Naval Medical Center.

FROZEN PLASMA

When liquid plasma, prepared by the same closed and scrupulous technic, is frozen within twenty-four hours after preparation at a temperature below -20° C., it may be preserved indefinitely, if stored below -15° C., without loss of any of the thermolabile constituents, such as prothrombin, complement and antihemorrhagic factor² ("plasma thromboplastin"). Thawing must be done in a water bath at body temperature (37° C.) with occasional shaking, and should not take longer than thirty minutes per bottle of plasma. It should never be attempted in an incubator. Thawing at a temperature below this level produces a massive fibrin precipitate, most of which goes into solution again if the plasma is promptly placed in a water bath at 37° C. A filter is not absolutely necessary if the frozen plasma is thawed properly, maintained at room temperature and administered within two or three weeks after thawing. However, inclusion of the filter in the intravenous set is a wise additional safeguard.

The plasma should be frozen in a near-upright position, a few bottles at a time, so that each bottle will freeze in less than three hours. A refrigerator containing a fan for circulating air over the cooling coils greatly accelerates the freezing. The plasma should then be stored in the horizontal position so that accidental thawing can be quickly detected. Precautions should be taken against discontinuance of the power supply to the refrigerator, and against too frequent opening of the refrigerator doors. It is advisable to have an available source of solid carbon dioxide (dry ice), should the power be discontinued and in the

event of mechanical breakdown. An internal-combustion engine can also be used in this exigency to run the compressor for the refrigerator. An alarm system should be installed in the refrigerator and adjusted to give a suitable signal when the temperature goes above -15° C.

Once accidental thawing has occurred, it is absolutely imperative that a good filter be used in the final administration set. There are three methods of handling this situation, none of which, however, prevents a certain amount of fibrin precipitation. If the refrigerator is operating, the plasma may be refrozen immediately, or thawing may be allowed to continue at 37° C. and the plasma stored as liquid plasma from that time on, or it may be then refrozen. In any event, much of the prothrombin and complement will be lost, and this advantage of preservation in the frozen state will therefore no longer exist.

DRIED PLASMA

The standard Army-Navy package of dried plasma can survive a wider range of temperature variation without denaturing or precipitating protein than can any of the other blood derivatives or forms of preservation. The package should not be permitted to freeze, nor should it be permitted to stand for any length of time above 55° C. (131° F.). If the plasma has recently been stored above 37° C. (98° F.), care must be taken to be absolutely certain that at the time of restoration the temperature of the water is not above 37° C., for in this event the proteins of the plasma may be either denatured or precipitated and untoward reactions may ensue. If the medical officer is in doubt concerning the maximum temperature to which the package has been subjected, he should be guided by the solubility time on restoration and the gross appearance after restoration. The solubility time should be less than three minutes with a small amount of shaking, and the gross appearance should be that of an opalescent or turbid solution without gross sediment, precipitation or gel formation.

Three hundred cubic centimeters of twice-concentrated plasma may be easily obtained using two standard Army-Navy packages of dried plasma. One bottle of plasma should be restored according to directions and used instead of the bottle of distilled water to restore the second bottle of plasma. In this manner the dried equivalent of 600 cc. of human citrated plasma will be dissolved in 300 cc. of distilled water.

Every medical officer who is expected to use plasma should familiarize himself with the directions of the restoration and administration of the standard Army-Navy package of dried plasma and follow them explicitly. The length of time

required to set up this package is a significant factor in the prognosis of a wounded patient. With a small amount of experience, the package can be opened, restored and prepared for administration in less than five minutes. The commonest error encountered is releasing the vacuum in the plasma bottle with the double-ended needle before this needle has been inserted in the water bottle. It should always be inserted in the water bottle before insertion in the plasma bottle.

The Subcommittee on Blood Substitutes of the National Research Council has recently recommended, and the Division of Biologics Control of the National Institute of Health has approved, the substitution of 0.1 per cent citric acid for the 0.1 per cent sodium chloride in the pyrogen free distilled water used at present to restore dried plasma. This substitution was recommended because of the observation that with the present methods of vacuum drying, restoration with a non-buffered neutral diluent produces an alkaline plasma.³ This alkalinity is relatively detrimental to such labile plasma constituents as prothrombin and complement. Restoration with a slightly acidified water will prevent destruction of these labile factors after reconstitution.^{2,3} This change has now been made in the standard Army-Navy package of dried plasma.

It has been believed for some time that it would be extremely desirable to include more plasma in the standard package. The majority of patients are now receiving an initial dosage approximating 500 cc., especially in the war zones. Accordingly, the package has been redesigned so that the amount contained will approach this figure.

In recent months, several communications⁴⁻⁶ have appeared in the medical literature concerning the alleged toxicity of plasma. A review of the results obtained from the plasma prepared at the Naval Medical School, and of the entire literature, has led us to the conclusion that the dangers from properly prepared pooled human plasma are practically nil. Thalheimer⁷ arrives at the same conclusion. Neither preliminary cross-matching nor skin-testing, both of which have been suggested by these critics, are, in our opinion, necessary. We have never observed a true hemolytic reaction following the use of pooled plasma, nor are we aware that one has been reported. Localized or generalized urticaria has followed the use of plasma in approximately 1 per cent of cases in our experience. This has invariably been easily controlled with subcutaneous adrenalin. The incidence of such reactions may be diminished but not eliminated completely by the use of fasting donors. If the untoward reaction rate from the administration of plasma exceeds 2 per cent, one

should be highly critical of the preparation of the equipment and the methods used in collecting blood and in aspirating, pooling and administering the plasma.

DOSAGE

The experience in this war with the use of blood derivatives in the prevention and treatment of shock due to trauma or burns has confirmed, beyond all question, the wisdom of administering an adequate amount early, preferably before the onset of symptoms of shock. In this, as in other military situations, error on the side of "too little

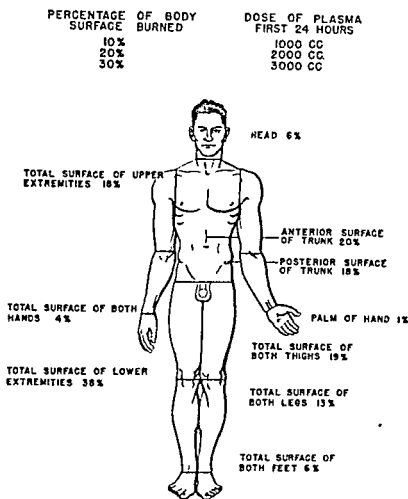


FIGURE 1. The Adjustment of Dosage of Plasma in Burns, according to Percentage of Body Surface Burned (modified from Berkou⁸)

and too late" is far more dangerous than "too much and too early." The possibility of the occurrence of irreversible physiologic and anatomic changes and death is directly proportional to the interval between injury and infusion with a blood derivative, and inversely proportional to the dosage used. There is also a direct relation between the amount of blood derivative required and the elapsed time after injury. Bearing these principles in mind will both decrease mortality and prevent waste of these precious materials.

Under the conditions imposed by modern warfare, the initial dosage of plasma or albumin must rest wholly on the judgment of the surgeon. Five hundred to 1000 cc. of plasma or 25 to 50 gm. of albumin is an advisable initial dose following a

severe injury or burn. An attempt should be made to utilize the laboratory aids of red-cell count, hemoglobin level, hematocrit and total protein content for the regulation of subsequent dosage, but the medical officer will frequently be forced to rely solely on the clinical response of the patient, including pulse and blood-pressure readings. In burns, a rough but useful rule for estimating the first day's dosage is to administer 100 cc. of plasma for each 1 per cent of the body surface burned, up to a maximum of 4000 or 5000 cc. Estimation of the area involved should be by Berkow's chart⁸ (Fig. 1). The knowledge that the palmar surface of one hand represents approximately 1 per cent of the total body surface is often very useful. When hemoconcentration has supervened, it has been advised⁹ that 100 cc. of plasma be given for every point the hematocrit is above 45.*

The use of whole-blood transfusions supplementing plasma or albumin may be of extreme importance in determining the prognosis of a wounded patient. The need for red cells may be masked initially by hemoconcentration. In burns, moderate anemia is prone to develop and is affected apparently only by blood transfusions.

The rate of administration of these derivatives should not exceed 10 cc. per minute for plasma or 5 cc. per minute for albumin unless clinical shock is present. In that eventuality it may be advisable to administer the material with double this speed.

INTRAVENOUS TUBING

In all medical establishments that prepare rubber tubing and glassware for drawing blood and

administering blood, plasma, albumin or other solutions, the personnel detailed to such preparation should be thoroughly conversant with the so-called "pyrogen-free" technic.^{11, 12} Unless such technic has been scrupulously followed, it is impossible to evaluate properly untoward reactions following intravenous infusions.

SUMMARY

Certain practical considerations relative to the use, abuse and storage of human serum albumin (concentrated) and liquid, frozen and dried plasma are briefly discussed. It is advised that medical officers familiarize themselves with these matters, lest an inordinate number of untoward reactions following the use of blood derivatives, and unnecessary waste of these precious materials, be permitted to occur.

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BIOPSY OF THE PROSTATE WITH THE SILVERMAN NEEDLE^{*}

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THE frequency with which carcinoma of the prostate occurs in elderly men has been recognized for a long time, yet the diagnosis is seldom made until the symptoms of urinary retention occur. For example, Rich¹ reported that in 292 consecutive autopsies in men over fifty 14 per cent showed carcinoma of the prostate, and in 65 per cent of these cases the diagnosis of carcinoma was not made during life. Since these cases were reported from the Johns Hopkins Hospital, it is obvious that, for the country as a whole, the percentage of unrecognized cases must greatly exceed this figure, especially in the older age groups, where the incidence of carcinoma of the prostate climbs rapidly to the astounding figure of 37 per cent. Because of the importance of this problem and because of one's inability to make the diagnosis by rectal palpation in early cases, and in a not inconsiderable number of more or less advanced cases, we began a year and a half ago to investigate seriously the possibility of prostatic biopsy.* Although from time to time most urologists have removed pieces of prostatic tissue for microscopic examination, few have realized the simplicity or value of routine biopsy with the Silverman needle. For this reason it has seemed worth while to present our results in 36 cases.

There are four ways of removing prostatic tissue for biopsy: by perineal exposure, by transurethral resection, by aspiration biopsy and by punch biopsy. Of these methods, the only one that can be followed as an office procedure and that removes an amount of tissue sufficient to be studied by the usual pathological technic is the punch biopsy. For this reason we have carried out punch biopsies, using the Silverman needle. Although this is only one of several instruments designed for this purpose, it has seemed to us, from a purely theoretical consideration, to be the most satisfactory.* We have had no experience with other methods of punch biopsy.

We admit that the best method is perineal exposure and biopsy under direct vision. This method, however, has one great drawback: it requires general anesthesia and about a week of hospitalization. It is ideal in those cases where perineal prostatectomy is indicated, since it can

be carried out as part of the operation to determine whether a partial or a total prostatectomy is required. However, in those cases in which perineal prostatectomy is not indicated, the magnitude of the procedure often results either in refusal of the patient to submit to the biopsy or in failure of the surgeon to recommend it. The removal of tissue for biopsy by transurethral resection has the same disadvantage in that it requires general anesthesia and at least some hospitalization. Another objection to this method is that the tissue removed must necessarily come from near the urethra, whereas the prostatic cancer most frequently originates near the capsule, where it cannot be reached by the resecting loop. Cases of carcinoma of the prostate are frequently seen in which the pathologist is unable to find evidence of malignancy in the tissue removed by transurethral resection. In this series there was 1 case in which 4 gm. of tissue had been removed by transurethral resection, with no evidence of malignancy having been found. However, since rectal examination of the prostate indicated a moderately advanced carcinoma, a biopsy with the Silverman needle was subsequently carried out. This showed malignancy, thereby establishing the diagnosis.

Although Ferguson² has reported excellent results with aspiration biopsy of the prostate and was able to remove tissue in from 78 to 86 per cent of his cases, we have not found this method satisfactory, for two reasons. In the first place, we have found it difficult to remove any tissue. In the second place, no pathologist who has not had extensive experience with the examination of material removed by aspiration biopsy is able to make a diagnosis, since the slide consists of nothing more than a smear of cells not unlike a blood smear. All the normal histologic arrangement is lost, and it is quite impossible to study the tissue or to grade the malignancy. On the other hand, although the amount of tissue removed by punch biopsy is small, it is large enough to fix and cut in the usual way. Thus it is possible for any pathologist not only to make the diagnosis, but also to make an estimate of the degree of malignancy and radiosensitivity.

The needle described in 1938 by Silverman³ has been used extensively by him and others to remove tissue from the liver, lungs and other organs, but has not, so far as we know, been used for prostatic biopsy. It is made in two lengths,

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and for this work the longer ($3\frac{3}{8}$ -inch) needle is necessary. The instrument consists of two parts: an outer 14-gauge needle, or cannula, and an inner needle, which is longer than the outer sheath and is split longitudinally from point to hub. The principle of operation is simple. The cannula is inserted up to, but not into, the suspected tumor.

real significance. A negative report merely means that the pieces of tissue removed show no malignancy, although other parts of the gland may be malignant. However, if four or more pieces of tissue, each measuring 1 by 10 mm., are obtained from every suspected prostate, an earlier diagnosis is possible than if one relies, as in the past,

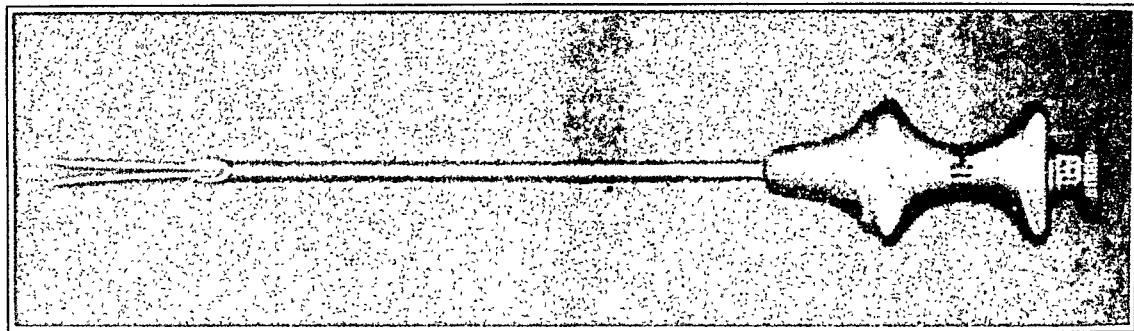


FIGURE 1. *The Silverman Needle.*

It is then held stationary while the inner needle is inserted through the outer one and into the mass from which a specimen is to be obtained. The split needle engages a section of the mass and holds it between its prongs. The outer cannula is then advanced over the prongs so as to cut off the piece of tissue and the entire instrument is removed. If this maneuver is properly executed a piece of tissue measuring 1 by 10 mm. is obtained. Since the piece is small it should be placed immediately on a piece of filter paper, which should be put in the fixing solution as soon as the operation has been completed.

In performing a biopsy on the prostate gland the patient is put in the extreme lithotomy position, the perineum is infiltrated with novocain, and, guided by a finger in the rectum, the needle is inserted to the desired spot. The accuracy with which this can be done depends entirely on how easily the prostate can be palpated, but unless the patient is excessively fat and nonco-operative this is not difficult. The only pain of which the patient complains is from the finger in the rectum. The biopsy can be accomplished without any help, but it is convenient to have an assistant hold the inner needle steady while the outer cannula is advanced so that several pieces may be cut without removing the finger from the rectum. None of our patients have had any reaction, and we have not hesitated to carry out the procedure on those who are ambulatory. In 3 cases we have inserted the needle too far and it has entered the bladder. In these patients there was slight hematuria but no other complications occurred.

In considering the value of prostatic biopsy, it must be realized that only positive reports are of

on simple rectal examination. In this series we have not succeeded in finding an early case of carcinoma of the prostate suitable for total removal, but this is, we believe, more a criticism of the medical profession as a whole than of the method.

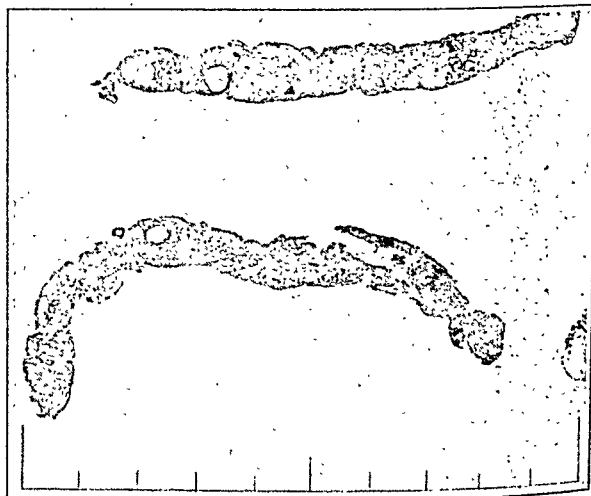


FIGURE 2. *Low-Power View of Specimens.*

These were obtained from a patient with benign hypertrophy of the prostate; the photograph shows their entire size. The markings on the lower edge of the cut represent one centimeter divided into millimeters. (Alcohol-formalin and celloidin technique; phloxine and methylene blue stain; magnification, $\times 18$.)

Seldom does one see early questionable cases of carcinoma of the prostate, but it seems likely that if it were generally realized that a simple technique exists by which the prostate gland can be biopsied, many more early cases would be referred to the urologist for diagnosis. In some cases, at

least, a positive biopsy would be obtained, a successful radical prostatectomy could be carried out, and a life would be saved.

However, aside from the question of early diagnosis, biopsy of the prostate has been of real

value in giving a prognosis and in enabling one to decide whether x-ray treatment is indicated, since some idea of the degree of malignancy and radiosensitivity can be obtained.

We have also found biopsy of value in planning the type of operation in cases in which there has been some doubt concerning the diagnosis, and in certain cases even negative evidence has been helpful. The greatest value of prostatic biopsy in this series, however, has been in confirming the diagnosis of carcinoma of the prostate in suspicious but not definitely proved cases in which, because of the lack of urinary symptoms, no operation was indicated. The fourth case of this series is a good demonstration of the value in this type of case. The patient had an unexplained edema of the left leg which his surgeon thought might be due to

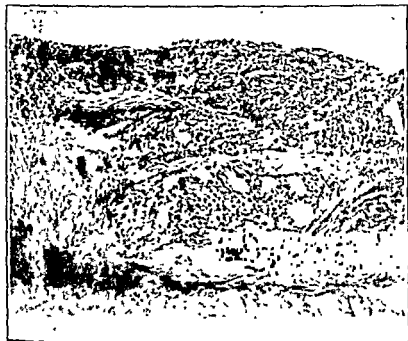


FIGURE 3. Low-Power View of a Specimen.

This was from a patient with a carcinoma of the prostate; it shows extensive infiltration of the stroma by moderately anaplastic, hyperchromatic tumor cells. (Zenker and paraffin technique; phloxine and methylene blue stain; magnification, $\times 160$)

value in a number of cases. For example, we have used this method to confirm the diagnosis of carcinoma before doing a bilateral orchidectomy. To be sure, in most of these cases the diagnosis can easily be made by rectal examination, but it seems desirable nevertheless to confirm it with a pathological diagnosis. In a recent case the patient returned to the Lynn Hospital six years after a transurethral resection. The original slides had been reported as showing carcinoma, but they were not available for re-examination. Cystoscopic examination showed no evidence of recurrence, and although the prostate felt hard on rectal examination, it was not enlarged. We were unable to make a positive diagnosis, and because of the long time that had elapsed since the operation, it seemed that the original diagnosis might have been incorrect. However, it was easily confirmed by biopsy, and a bilateral orchidectomy was done. In the cases of carcinoma of the prostate treated by orchidectomy we hope to repeat the biopsy at a later date, and by comparing the two slides to learn something about the histologic changes that occur in the malignant gland following removal of the testicles. From the research point of view, this appears to be an ideal way of studying the effect of various hormones on the gland. Biopsy is also of value in



FIGURE 4. High-Power View of an Area of the Section Shown in Figure 3 (magnification, $\times 450$).

metastases from a malignant prostate. We made a careful rectal examination and reported that we did not think the patient had carcinoma of the prostate. However, since we were interested in seeing what could be accomplished with the needle, we did a biopsy on the prostate gland. Much to our surprise, the removed tissue showed carcinoma. The subsequent course of this case has proved the diagnosis to be correct. There was an interesting medicolegal angle to this case, since the patient later claimed that his disability resulted from an accident. The prostatic biopsy was of considerable importance to the insurance company in proving that this was not so. In several other cases the biopsy was of distinct value in confirming the diagnosis of carcinoma where it had been suspected from the x-ray findings or other evidence but could not be proved by rectal examination.

We have carried out biopsies in cases with the following

were reported as carcinoma. The diagnosis in all these cases has been proved to be correct, either by the examination of tissue removed at operation or by the subsequent course. In 17 cases the tissue showed no evidence of carcinoma. Five of these cases were not operated on, and in 10 cases the diagnosis was proved correct by operation. In 2 of the 17 cases the diagnosis was incorrect, since the patient had carcinoma of the prostate. One of these cases had a second biopsy that was positive. In 3 cases we failed to remove a satisfactory amount of prostatic tissue for examination. These cases need further comment. We had no difficulty in removing tissue from the first 13 cases in which we attempted a biopsy. However, after the needle was broken in an attempt to biopsy a bone tumor, we commenced to experience difficulties. We subsequently discovered that these needles are all made by hand and without definite specifications, so that no two are alike. A small variation in their construction or the type of steel used makes a considerable difference in the ease with which the tissue can be removed. The manufacturer has been co-operating with us and this technical difficulty seems to have

been corrected, so that in the future we expect to be able to remove adequate amounts of tissue in every case. It has been our experience that in a hard, malignant gland there is never any difficulty in removing an adequate amount of tissue. Since this is the type of gland one is most anxious to biopsy and the most difficult to handle by aspiration biopsy, the relatively few failures do not detract greatly from the value of the needle.

SUMMARY

The Silverman needle was used to biopsy the prostate gland in 36 cases, with satisfactory results in 86 per cent. As a means of removing tissue this method is safe and simple, and is applicable to ambulatory patients. It is of value not only as an aid to the early diagnosis in carcinoma of the prostate, but also in establishing or confirming the diagnosis.

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MEDICAL PROGRESS

SKIN CHANGES OF NUTRITIONAL ORIGIN*

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NUTRITION is becoming an increasingly complex and important subject. Almost every vitamin deficiency has been produced experimentally in human beings in pure form and the resultant clinical manifestations have been carefully studied. Experimental specific amino acid deficiencies in human beings¹⁻³ have likewise been produced. The results of these definitive experiments indicate that there is often a considerable overlap in the clinical syndromes produced by each pure deficiency. Symptoms and signs commonly considered specifically diagnostic of certain deficiencies are beginning to assume new or additional meanings. Likewise, failure of a number of manifestations attributable to vitamin deficiencies to respond to the recommended therapy has emphasized anew that there are etiologic back-

grounds for disease other than vitamin deficiencies.

There have been numerous reviews describing the clinical pictures of the various vitamin deficiencies. A novel and helpful approach to this general subject is to consider some one area of the body, describe its specific anatomy and function, and relate how vitamin deficiencies as well as other etiologic factors influence it. In last year's progress report the tongue changes seen in nutritional deficiencies were reviewed with that approach. The present review deals in a somewhat similar manner with a number of skin changes of nutritional origin. The subject is a pertinent one in view of the rapid advance in the use of vitamin therapy in the field of dermatology.⁴⁻¹⁵

CAROTENEMIA AND CAROTENODERMA

In spite of the widespread use of vitamin preparations during the last ten years, the scarcity of reports of untoward effects of excess vitamin in-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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The carotenoid group of pigments color the serum and fix themselves to the fat of the dermis and subcutaneous tissues, to which they impart the yellow tint. They are deposited in the horny layer (stratum corneum) of the epidermis and in the sebaceous glands.^{24, 31} Edwards and Duntley³² showed by means of spectrophotometric analysis of skin color in human beings that carotene is present in every normal skin and is one of the five basic pigments that determine the skin color of every living person. Clinically, therefore, carotenemia refers to the presence of an excess over normal of carotene in the skin and serum.

The ease with which the yellow pigmentation of the skin in carotenemia has been misdiagnosed as, or confused with, jaundice has been a major theme in the numerous papers on this subject. In most cases carotenemia results simply from excess use of foods rich in the carotenoid pigments. Individuals probably vary in the ease with which carotenemia develops, which is evidenced by the fact that many vegetarians do not develop it.³⁰ It is said to develop more readily in those who sweat profusely. Except for the yellow color produced, it appears to be harmless, even though present for months. It eventually disappears over several weeks to months when the carotene consumption is reduced. Carotenemia may readily appear when large doses of pure chemical carotene are used medicinally as a source of vitamin A.³³ Here, likewise, it is harmless and disappears slowly when the carotene dosage is reduced.

Carotenemia is frequent in diabetic patients. Boeck and Yater²² found the blood carotene increased in 86 per cent of 100 such patients studied; however, only 10 per cent had a detectable yellow pigment in the skin. Stueck, Flaum and Ralli³⁴ report a study of 13 diabetic patients with clinical evidence of carotenemia. Other similar studies emphasizing this frequency in diabetic patients^{35, 36} have been made. It is believed to be due both to the high lipochromic diet used and to the diminished conversion of carotene to vitamin A in the liver.²⁴ Because of the frequency of this condition in diabetic patients, the finding of carotenemia necessitates considering diabetes mellitus as a possible cause.²¹

Patients with kidney disease may manifest some degree of carotenemia, possibly owing to poor urinary excretion of this pigment; this is a point by no means agreed on. Boeck and Yater²² noted xanthosis (carotenoderma) in 10 per cent and xanthemia in 100 per cent of their kidney cases. However, the pigmented element of the yellowish pallor noted in uremia may be due in part to retention of urinary chromogens that are oxidized in the exposed portions of the skin

to the corresponding yellow pigments, the accompanying pallor being due to the anemia so frequent in uremia.³⁷

The recent reports by Escamilla³⁸ and Mandelbaum et al.³⁹ confirm earlier observations^{21, 40} that the yellowish color so frequently noted in myxedema is due to carotenemia, which may occur in this disease even when the amount of carotene in the diet is low. According to Escamilla, the conversion of carotene to vitamin A in the liver is hindered by the depressing effect of the lowered metabolism and tends to improve gradually under treatment with thyroid substance. Escamilla also mentions the opinion held by Stepp and Wendt that the thyroid hormone is antagonistic to vitamin A and governs the rate of its consumption. In hyperthyroidism the consumption is accelerated and the rate of change from carotene to vitamin A is increased, with resultant low serum carotene, whereas in hypothyroidism the opposite is found, the vitamin A in the serum remaining normal or low whereas the carotene is increased. Carotenemia was likewise noted in a case of Simmonds's disease, probably due to a similar mechanism of lowered metabolism.³⁸ Edwards and his co-workers⁴¹ using spectrophotometric analysis of skin color, found an excess of carotene in the skin of castrate and eunuchoid men, which reverted to normal on treatment with testosterone propionate.

A therapeutic curiosity has been reported by Bendes,⁴² who put carotenemia to a practical use. Blond tuberculous children were fed vegetables in abundance. The resultant carotenoid pigmentation of the skin protected them from blistering during heliotherapy and facilitated tanning of the skin.

Carotenemia may be present in liver disease owing to failure of that organ to convert the provitamin carotene to vitamin A, but may be readily masked by the accompanying jaundice. The three-layer test of Greene and Blackford²¹ allows the laboratory demonstration of excess carotene in the serum even though excess bilirubin is also present.

Being a fat-soluble substance, carotene is poorly absorbed in obstructive jaundice and sprue.⁴³ Likewise, the presence of mineral oil in the gastrointestinal tract interferes with the absorption of carotene.⁴⁴ Hyperthyroidism can lower blood carotene.³⁸ Under such circumstances the blood-carotene level may be less than normal. Similarly low blood-carotene levels may result when the food intake of carotene is low. Such conditions may contribute to vitamin A deficiency, especially when preformed vitamin A is not present in adequate amounts. Little if any attention has been paid to the skin color when the blood and tissue caro-

tene is less than normal. Such changes are probably of no clinical significance as regards skin color, but are undoubtedly significant in relation to the production of vitamin A deficiency.

Carotenemia has been experimentally produced many times in human beings by excess consumption of carotene-rich foods.²¹ Determination of the time required to produce carotenoderma under clinical circumstances has been difficult to evaluate for obvious reasons. Almond and Logan²⁴ state that 4 pounds of excess carrots per week for seven months are necessary. Wood and Agnor⁴⁵ mention a patient who ate two carrots daily for a year. Rosen's⁴⁶ patient weekly ate two bunches of carrots for a year. I have seen one clinic patient with carotenemia who had a history of eating pumpkin or squash pie daily for several months. A youth of twenty with carotenoderma seen at an army induction station had eaten several large carrots daily for about seven months. Some time previously he had read that carrots improved aviator's vision for night flying. He had eaten the carrots in anticipation of making a "good showing" in the eye tests when he applied for the Army Air Corps. All these statements refer to items additive to an average diet. A perusal of the dietary history of recorded cases reveals that a wide variety of foods, taken in variable amounts for a varying duration, have been responsible. In general, the time has been one of months rather than of weeks. These factors and varying individual susceptibility make it difficult to predict how much pigmented food a normal person must eat to develop a significant degree of carotenemia.

Children are said to develop carotenemia more readily than do adults. Hess and Myers²⁰ produced carotenemia in infants by feeding two oranges, an egg, or 2 ounces of spinach daily for a month. They noted, as have others since, an individual variation in susceptibility to the accumulation of carotenoid pigments in the blood.

Of special interest in Almond and Logan's²¹ paper is the infant who developed carotenoderma after only two months on the breast milk of its carotenemic mother. Pariente, Present and Ralli²⁶ mention that De Buys reported the case of a carotene-pigmented baby born to a carotenemic mother, the child remaining yellow until weaned.²⁶ The carotene pigment is present in breast milk, whereas bilirubin is usually not.

Almond and Logan²¹ in England report their observations on 4 women who showed such a pronounced carotene pigmentation of the skin that a tentative diagnosis of hemolytic anemia, pernicious anemia or obstructive jaundice was at first considered. In each case excessive amounts of

Their report emphasizes once more the ease with which carotenemia may be confused with jaundice. This is the main reason why every physician should be familiar with the clinical picture of carotenemia and the specific features which distinguish it from jaundice.

The eating habits of a nation change with time. Rationing in this country will result in the consumption of more fresh vegetables and less butter, cheese and so forth. It is possible that carotenemia may become more prevalent in the United States than in the past. It is a condition worth considering in the differential diagnosis of any obscure, long-standing case of mild jaundice.

Excess carotene is in part excreted in the sweat and reabsorbed by the horny layer of the skin. Characteristically the yellow pigmentation is noticeable first and predominantly in the nasolabial folds and over the forehead, where sebaceous glands abound, and in the palms and soles, where the horny layer of the skin is the thickest.²¹⁻²⁴ According to a case reported by Gandy,³⁰ "in the palms and soles the tinting was deepest on the outer edges, a classical feature." A lighter degree of accentuation of pigmentation may be noted in the upper eyelids, the inner canthi, the ears, the anterior folds of the axillae and over areas subject to pressure, such as the elbows, knees and heels.³⁰ This uneven distribution of the carotene pigment in the skin of persons with carotenemia is more noticeable than variations in the distribution of bilirubin pigment in the skin of jaundiced patients. When the carotenemia is long-standing and severe, the rest of the body skin may become pigmented.

Many patients have mild degrees of carotene without a detectable carotenoderma. The blood carotene threshold necessary to produce visible carotenoderma is not clear. In one experiment Pariente and his co-workers²⁶ noted carotenoderma when the blood-carotene level reached 0.54 mg. per 100 cc., whereas it was 0.50 mg. for 3 diabetic patients with carotenoderma. Stueck, Flaum and Ralli²⁷ noted clinical carotenoderma in each of 10 diabetic patients with serum-carotene levels varying from 0.21 to 0.8 mg. per 100 cc. and averaged 0.39 mg. They mention the average normal serum value as 0.11 mg. This suggests that carotenoderma may be noted when the serum-carotene level reaches two to five times the normal value.

The yellow color of carotenemia has been variously described as canary, lemon, ocher or golden,²¹ canary yellow being perhaps the common term used. It never manifests the bronze, orange or green tint of jaundice. The serum carotenemia is described as yellowish to orange-yellow and particularly

main white, in contrast to the early and marked presence of bilirubin in this area in true jaundice. Subconjunctival or submucosal fat, if present, may be stained, however, and lead to confusion. Attention must be paid to this clinical minutia if one wishes to use the appearance of the scleras or mu-

if the potassium dichromate color standards are used. The three-layer test of Greene and Blackford²¹ enables the diagnosis of carotenemia to be made, even when excess bilirubin is present in the blood. Equal quantities of serum, alcohol and petroleum ether are shaken in a tube, and on stand-

TABLE 1. *Differential Features of Carotenemia and Jaundice.*

DIFFERENTIAL FEATURES	CAROTENEMIA	JAUNDICE
Pigment responsible for the yellow color	Carotenoid (lipochrome) pigments	Bilirubin
Areas where pigmentation is first noticed	Forehead, nasolabial folds, palms, soles and over pressure areas	Scleras, mucous membrane under tongue, and body areas with thin skin
Extent of pigmentation when of severe degree	Entire skin with accentuation in areas mentioned above	Entire skin, scleras and mucous membranes least on palms and soles
Scleras	Free of pigment	Pigmented
Mucous membranes	Usually free of pigment	Pigmented
Color of pigment	Canary or lemon yellow	Yellow with green, bronze, orange or saffron tint
Urine	No significant color change	Except for "retention" jaundice, dark from presence of bilirubin
Stool	No change	Clay colored in obstructive jaundice, normal or darker in other types of jaundice
Icteric index (potassium dichromate standards)	Increased	Increased
Blood bilirubin (quantitative van den Bergh test)	Normal	Increased
Greene and Blackford's three layer test	Lipochrome yellow pigments in top petroleum ether fraction	Yellow bilirubin pigment in center alcohol layer
Dietary history	Excess ingestion of foods rich in carotenoid pigments	Generally not significant as an etiologic background
Diseases accentuating or responsible for its production	Diabetes mellitus, kidney failure, myxedema, liver disease and possibly other endocrine disorders	Except for liver disease, other diseases responsible for carotenemia do not as a rule cause jaundice
Itching of skin	Not present	Frequent
Effect on health	No effect on health	Almost always a serious condition
Duration	Lasts as long as foods rich in lipochromes are consumed in excessive amounts (weeks to months or more)	Varies with type of jaundice
Time required to produce disease	Several months of excess ingestion of foods rich in lipochrome pigments	Days to weeks
Transmitted by breast milk to nursing child	Yes	No

cous membrane as a differential point. A paper by Wise and Diasio²⁹ contains four remarkable full-page colored plates showing the appearance of the face, palms, soles and serum of a patient with carotenemia. A perusal of these plates will be worth while for anyone not familiar with this clinical picture.

Carotene causes no feeling of ill-health except the anxiety occasioned by the skin discoloration; this is particularly true if an erroneous diagnosis is made to explain the "jaundice." Itching, so commonly present in jaundiced patients, is absent in carotenemia.

Carotenemia does not significantly change the color of the urine or of the stools. Almond and Logan²⁴ attempted extraction of the yellow color of the urine from their patients with petroleum ether, without success. The urine was said to have been deep orange in some of their patients.

The yellow color of the serum due to excess carotene may be confused with hyperbilirubinemia

ing separate into three layers; the top layer of petroleum ether contains the lipochrome pigments, the middle alcohol layer bears bilirubin, and the serum proteins are precipitated in the bottom layer.

The pertinent differences between carotenemia and jaundice are summarized in Table 1.

PHRYNODERMA

Vitamin A deficiency in man results in impaired dark adaptation of the eyes (night blindness), dryness of the cornea and conjunctivas (xerosis, or xerophthalmia when severe) and a characteristic skin change (phrynoderma), as well as certain systemic changes.

Most patients are unaware of their night blindness, its detection being possible only by means of a dark-adaptation test. As a rule it responds rapidly (within days) to vitamin A therapy. Severe xerophthalmia is rare in this country. Mild xerosis is common; it may be symptomless and not readily

detected clinically. It usually responds well to therapy.

The specific cutaneous lesions considered characteristic of vitamin A deficiency were first recognized and described in 1931 by Frazier and Hu⁴⁷ in China. Their observations have been amply confirmed, and many descriptions of similar lesions seen in this country are now on record.⁴⁸⁻⁵³

The early change is one of simple dryness (xeroderma).^{48, 53} When more severe, according to Markowitz,⁵⁴ the normal skin epithelium atrophies and is replaced by proliferating basal cells that become keratinized. A similar process in the skin glands and ducts causes accumulation of keratinized epithelium, which by protruding from the pilosebaceous follicular orifices results in the hyperkeratotic papules (hyperkeratosis follicularis) so characteristic of this disorder. Sebaceous-gland and sweat-gland function is diminished. The papule is commonly 1 or 2 mm. in diameter, but may in severe cases be as large as 5 mm.⁵³ It gives the skin a rough, grater-like feel, detected more easily by palpation than by inspection when mild, but readily noticeable if severe. The follicular papules are most prominent on the neck, back, buttocks, calves, elbows, knees and the posterolateral aspects of the upper arms and thighs. Dryness of the scalp is common. The lesions when present on the face resemble acne but are not pustular⁴⁸; they are not frequent in this location.

The skin may become quite pigmented, a finding common in Negroes and Asiatics⁵⁵ but evidently a rarity in the white race.⁵⁶ Itching may occur⁵³ and at times be extremely severe.⁵⁷ There may be loss of hair in the severely involved areas. A gaping hole is left if a papule is pulled out of a follicle. Broken-off hairs or coiled, unerupted hair may be contained in the papule. This papular eruption has been called "goose-skin" because of its resemblance to cutis anserina ("goose pimples"), produced by reflex contraction of the erector pilorum muscles. The term "phrynoderma" (meaning "toad skin") introduced by Nicholls⁵⁸ is most descriptive of the dermal manifestations of severe avitaminosis A and already has wide usage. Markowitz⁵⁴ refers to it as "Frazier and Hu disease." However, a more appropriate eponym, if one is to be used, is "the Frazier and Hu syndrome," since follicular hyperkeratosis also occurs in scurvy. Keratosis pilaris of the dermatologic literature and its synonyms, lichen pilaris, lichen spinulosum, ichthyosis follicularis and so forth, are believed to be descriptive terms for the cutaneous manifestations of phrynoderma.⁵³

Frazier and Hu⁴⁷ believed that avitaminosis A

rarely occurring before sexual maturity. Le and Rapaport⁵³ point out that this impression though widely held, needs revision, and on basis of their own experience added to impression support from the literature state that follicular lesions are not infrequently found among privileged children.

Lehman and Rapaport⁵³ studied the families of the children whom they noted to manifest phrynoderma, and were surprised at the frequency with which it occurred in other members of the families. This familial occurrence may have been due to the fact that all the families consumed deficient diet. These authors remarked, however, that "some hereditary disturbance in vitamin metabolism, interfering with the utilization of vitamin A, or producing an increased requirement for this substance, may be considered also."

In contrast to the rapid improvement usually noted for night blindness, phrynoderma responds poorly to therapy, two to four months or longer of vigorous therapy being the usual requirement.^{49, 60} Straumfjord⁵² has noted some patients who, after four years of continuous oral therapy, showed only partial subsidence. The very chronicity of phrynoderma readily allows a person to get in and out of mild deficiency superimposed on the background of chronic skin changes completely relieved. This probably accounts for the frequent inability to detect night blindness when what otherwise seems like a case of vitamin deficiency. While working at an army nutrition center, I have been impressed by the chronicity with which varying degrees of phrynoderma and even mild ichthyosis have been noted in a cross section of the young adult male population. On most occasions, questions relating to subjective night blindness were answered in the negative. A photometer test would have been required to detect the night blindness. Many degrees of follicular hyperkeratosis are usually overlooked,⁵² or else not treated vigorously enough or long enough to obtain a satisfactory therapeutic response.

The specificity of these lesions as indicating avitaminosis rests on their frequent association with the same person with xerosis and impaired adaptation, careful dietary histories of intake of vitamin A and response to vitamin A therapy in addition, they have been produced in humans kept on an experimental vitamin A deficiency diet.⁶¹⁻⁶³

Keil⁶⁴ has reviewed the earlier literature tending that hyperkeratosis follicularis may

were commonly called "scorbutic goose flesh" and "lichen scorbuticus." The common criticism of this idea has been that these scurvy patients had an unrecognized accompanying vitamin A deficiency. The question appears definitely answered by the appearance of these lesions in Crandon⁶⁶ during his six-month period of self-induced pure scurvy. I had the opportunity to examine Crandon's hyperkeratotic follicular lesions, and noted them to resemble in every way those described in the literature on avitaminosis A. I was also able to compare them with similar ones that developed in a patient whom I had placed on an experimental vitamin A-free diet.⁶³ Crandon's skin became dry and slightly rough, and the hairs fragmented easily and often grew abnormally in the follicle, all of which are changes that are seen in vitamin A deficiency. Crandon's dark-adaptation test and his blood vitamin A level were both normal. Besides, he took 30,000 international units of vitamin A daily throughout the experiment. It thus appears evident that hyperkeratosis follicularis may be seen in both scurvy and avitaminosis A. Until the red perifollicular areola or perifollicular hemorrhages develop in scurvy they cannot be told apart—a differential point emphasized by Machella.⁶⁷

The "shark-skin" appearance of the filiform excrescences of inspissated sebum on the faces of pellagrins and riboflavin-deficient persons may also be confused with phrynoderma. However, the primary localization in the face, the seborrheic skin and the absence of the excrescences on the extremities rule out phrynoderma.

Field and his co-workers⁶⁸ have emphasized the frequency with which patches of hyperkeratosis appear over the pressure areas (elbows, knee, soles and so forth) in the type of chronic pellagra seen in the northern part of this country. Callus formation was also common. These changes responded to therapy specific for pellagra. Such areas of hyperkeratosis may be confused with some aspects of the phrynoderma of avitaminosis A.

Moorc, Spies and Cooper⁶⁹ noted hyperkeratosis of the skin in the histologic study of skin specimens from pellagrins, and concluded that a deficiency in the vitamin B complex produced a disturbance in keratinization.

The pathogenesis of phrynoderma is not clear. Vitamin A is not present in the epidermis, even though this layer of the skin is especially sensitive to its deficiency.⁵⁴ Cornbleet and Popper,⁷⁰ utilizing a special fluorescence and microscopic technic, were able to demonstrate it only in the underlying fat cells. It did not appear in the epidermis, even with a high intake of vitamin A.

Carotene is present in the epidermis³¹; supposedly, however, it cannot function locally without conversion to vitamin A.

The factors that determine the deposition, mobilization and distribution of vitamin A in the body are largely unknown.⁵² Since vitamin A, unlike vitamins B and C, is not water-soluble, it cannot readily diffuse in tissue fluids. Since it is present in the blood, the adequacy of the blood supply to a given region may also determine the amount of vitamin A furnished, lesions being unlikely to develop where the blood supply is abundant and being of common occurrence in areas with decreased circulation. Straumfjord⁵² uses the aforementioned premises to explain the characteristic distribution of the follicular hyperkeratosis on the back, elbows, buttocks, calves and the posterolateral aspect of the thighs and arms. He points out that these are the body surfaces on which the weight of the body rests during sleep and sitting, and that the resultant mechanical pressure of the body weight diminishes the blood flow and therefore the supply of vitamin A to the areas involved, with resultant localization there of the lesions. Straumfjord⁵² believes that corns and callosities may in some cases represent a localized dyskeratotic epidermal change due to a similar pressure mechanism. He reports that in some of his patients taking 100,000 international units of vitamin A daily for long periods (several months to three years) the disappearance of corns and callosities was observed even though present in the same skin areas for many years before treatment was commenced. Whether ingested arsenic that is deposited in the skin may not combine with vitamin A carried there by the blood, thus explaining the follicular hyperkeratosis and palmar and plantar keratoses that develop in certain persons following the administration of arsenicals is another query raised by this worker.

KERATOSIS FOLLICULARIS (DARIER'S DISEASE)

The standard textbooks on dermatology describe Darier's disease as an obscure chronic skin disorder, commoner in males than in females, commencing early in life, at times demonstrating a familial tendency,⁷¹ and characterized at first by discrete, firm, keratotic follicular papules of the same color as the skin. With time the papules become darker, turning red and then brownish or purplish, coalesce, and form papillomatous masses. The eruption is symmetrical and widespread. The palms and soles become horny and thickened. Although the skin disorder is chronic and usually intractable to treatment, the general health remains unimpaired.

The resemblance of this disease to the skin manifestations described for avitaminosis A have not gone unnoticed. Peck, Chargin and Sobotka⁷² present convincing evidence linking the pathogenesis of this disorder to some abnormality of vitamin A metabolism. They studied in detail

Darier's disease represents a disorder attributable to an abnormal metabolism of vitamin A. Heritance of Darier's disease may represent in part this metabolic abnormality. It should be emphasized that the skin usually improves but did not become entirely normal. This

TABLE 2. Results of Treatment of Keratosis Follicularis (Darier's Disease) with Vitamin A

Author	PATIENT		DAILY U.S.P. UNITS OF VITAMIN A ORALLY	DURATION OF TREATMENT	EFFECT ON SKIN LESIONS
	AGE	SEX			
Welton ⁷⁴	29	F	80,000-100,000, finally kept on 200,000	About 1 yr	Definite clearing up, and increased pliability of definite subjective improvement
Newman ⁷⁵	19	F	150,000-25,000	5 wk	Almost complete resolution of the eruption
Barwasser ⁷⁶	38	M	200,000	4 mo	Disappeared from less rest of body greatly improved
McKelson ⁷⁷	26	M	25,000-240,000	5 mo	Improvement
Sweitzer ⁷⁸	82	M	100,000	2 mo	Decided improvement
Peck ⁷⁹	27	M	200,000-250,000 orally, also 100,000 intramuscularly	9 mo 2 mo	Decided resolution with relapse during the months
McKelson ⁸⁰	25	F	320,000-250,000	2 mo	Much improvement
Abramowitz ⁸¹	30	F	100,000	4 mo	Consistent regression except on palms and soles
Haynes ⁸²	41	M	100,000	1 mo	Definite improvement

4 patients with Darier's disease, not only utilizing the clinical responses to vitamin A therapy but also following the blood vitamin A and carotene levels, and in 2 cases the dark-adaptation curves as well. They showed clearly that night blindness occurs in patients with Darier's disease. The eruption in 3 cases improved when massive vitamin A therapy was given orally over a considerable period. In all 4 cases the patients, while on a diet that contained a normal amount of vitamin A, showed a decided decrease in the vitamin A content of the blood serum even though the blood carotene level was normal. This suggested that there might have been a hereditary weakness in vitamin A absorption or in conversion of provitamin A (carotene) to vitamin A. Massive doses of vitamin A given orally raised the blood vitamin A to normal, but it became low again when this therapy was discontinued. Curiously enough, massive intramuscular doses seemed to lower the blood vitamin A level.⁷³ Peck⁷³ mentioned later that excessive vitamin A intake (over 300,000 international units) might make the keratotic papules become bullous. Welton's⁷⁴ observations of a patient confirm in general the findings of Peck and his co-workers with regard to the blood findings of the carotene and vitamin A blood levels.

There are now on record the results obtained by various physicians who have treated Darier's disease with massive doses of vitamins.⁷⁵⁻⁸² These supportive data, given in Table 2, emphasize the magnitude of the vitamin dosage used and the duration of the time over which it must be administered. On the whole the results have been favorable and seem to support the belief that

gists that there may be other factors in the pathogenesis of Darier's disease in addition to impaired vitamin A metabolism.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

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CASE 29211

PRESENTATION OF CASE

A fifty-three-year-old housewife was referred to the hospital because of a generalized skin rash and marked oliguria.

Approximately three months prior to admission the patient noticed a fissure at the tip of the right nostril. Her physician prescribed sulfathiazole ointment, which she applied for several days every two or three weeks during which time the lesion temporarily healed, only to recur. Eleven days before entry her physician prescribed sulfathiazole by mouth, of which she took 4.5 gm. in thirty-six hours without improvement. The sulfathiazole was then increased to 1 gm. every four hours for the succeeding twenty-four hours, following which a generalized skin eruption developed. At that time her temperature rose to 102°F. and edema and swelling developed about the eyes. The sulfathiazole was discontinued and the patient was admitted to a community hospital. There the patient received 2 gm. of sulfathiazole as a test dose. This was followed in several hours by an exacerbation of the skin eruption and a rise in the temperature to 104°F. During the three days prior to admission she vomited several times, and two days before entry the urinary output was found to be 100 cc. per day. No sulfonamide crystalluria was known to have occurred.

The past history showed that the patient had always been well. Five months prior to admission she had an attack of "acute asthma." The cardiovascular history was not remarkable, except that she had had nocturia (once) for five years. One year was frequently troubled with "hives."

Physical examination disclosed an obese, constricted woman who seemed quite ill. The breath was not acidotic. Involving the face, neck, upper trunk and lower legs, was a rash that, in its early form, was dull, erythematous and maculopapular, with central nodules. Some of the lesions seemed to be hemorrhagic blebs; others were pustular and crusted. There was dullness at the bases

of both lungs posteriorly, and fine crackling rales were audible as high as the scapulas. The heart was normal. The abdominal panniculus was very heavy. No abdominal masses were felt, and there was no costovertebral angle tenderness.

The blood pressure was 130 systolic, 64 diastolic. The temperature was 102°F., the pulse 110, and the respirations 21.

Examination of the blood revealed a hemoglobin of 14.3 gm., and a white-cell count of 27,200, with 95 per cent neutrophils, 3 per cent lymphocytes and 2 per cent monocytes. The red-cell count and platelets were normal. The urine was cloudy orange and acid, and gave a + test for albumin; the sediment contained many white cells and granular casts, 10 red cells and 13 epithelial cells per high-power field, and a great deal of amorphous debris, no crystals being seen. The nonprotein nitrogen was 64 mg. per 100 cc., and the chloride 76.3 milliequiv. per liter. The blood sulfathiazole was 2.2 mg. per 100 cc. Cultures of the skin lesions were negative.

A chest roentgenogram revealed areas of atelectasis in the lower lung fields. There was no gross consolidation. The heart appeared prominent in the region of the left ventricle, and the aorta was slightly tortuous.

Irregular fever continued for four days, but was subsequently normal. The pulse was usually 80 to 90 during hospitalization. Daily infusions of 1500 cc. of glucose in distilled water were given. The nonprotein nitrogen gradually rose; the patient felt nauseated and seemed somewhat disoriented. On the fifth hospital day the skin seemed improved. The nonprotein nitrogen was 99 mg. per 100 cc. The carbon dioxide combining power was 21 millimols and the chloride 71.9 milliequiv. per liter. The patient seemed short of breath but examination of the lungs was not remarkable. The white-cell count was 12,500. The daily urine specimen totaled 30 cc., was acid, had a specific gravity of 1.010 and showed a ++ test for albumin and a light-green sugar test; a test for diacetic acid was negative. The sediment contained 15 red cells, 40 white cells, 10 round cells and 6 epithelial cells per high-power field; no crystals were seen. Examination of the nose and throat on the sixth day revealed a subacute nasal pharyngitis. After removing thick, mucopurulent, stringy material, approximately 15 cc. of thin, frankly purulent material was aspirated from the nasopharynx. The mucous membrane was inflamed throughout. Oral hygiene was extremely poor, with large, dry, brown crusts throughout. On the sixth hospital day the nonprotein nitrogen was 144 mg. per 100 cc.; the chloride was 65 milliequiv., and the carbon dioxide combining power

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mention about pigmentation and so forth, and it seems to me the whole story is that of renal, not adrenal, failure.

So I come down to a diagnosis of sulfathiazole nephritis with fatal termination.

DR. TRACY B. MALLORY: Conversations with my lay friends lead me to believe that many doctors now hand out tubes of sulfathiazole ointment and tell their patients to apply it every time they scratch their skin. I think it certainly is quite possible that any patient could be sensitized in that manner.

DR. JACOB LERMAN: How do you explain the low chloride, Dr. Richardson?

DR. RICHARDSON: On the basis of vomiting. I meant to mention that. I should have thought they would have given physiologic saline instead of distilled water.

DR. LERMAN: There is no mention of the blood-sodium level. She may have lost a lot of sodium by perspiration.

DR. RICHARDSON: That brought up in my mind the adrenal bugbear, but I think I shall throw it out.

CLINICAL DIAGNOSIS

Sulfonamide nephrosis.

DR. RICHARDSON'S DIAGNOSIS

Sulfathiazole nephritis.

ANATOMICAL DIAGNOSES

Sulfonamide interstitial nephritis, with granulomas.

Acute myocarditis.

Pulmonary edema.

Subacute and chronic pancreatitis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This case was tremendously important, and we had great difficulties in regard to post-mortem examination; Dr. Maisel eventually drove a hundred miles to perform the autopsy in an undertaker's parlor. It turned out to be worth while, since the kidneys are the most interesting we have seen.

The pair of kidneys weighed 650 gm., each kidney alone being the size of a normal pair of kidneys. The body had already been embalmed so we did not have a chance to see the kidneys in a fresh state. But even after embalming it was evident that they were markedly discolored, with very pale patches alternating with areas of hemorrhage. The change was most marked in the cortices, which were extremely swollen. The pelvis showed no crystals, and even when the kidneys

were examined under the dissecting microscope we could not find any crystals. Microscopic examination of the kidney showed an extreme degree of edema of the cortex and a very diffuse infiltration of lymphocytes, with a moderate number of plasma cells. There were so many inflammatory elements that at first glance one thought of pyelonephritis, but the infiltration was limited to the cortex and did not involve the pyramids. It was clear that the changes were not due to pyelonephritis. In addition to this diffuse infiltration there were small granulomas in the interstitial tissue, such as Maisel¹ has described in experimental cases of sulfonamide poisoning. I think I am correct in saying that he had not seen any case with the diffuse change that was present in this renal cortex. It is reminiscent of the entity that used to be called interstitial nephritis, which, in the period from 1895 to 1910, was a common finding in patients with scarlet fever, but which has almost completely disappeared as a disease at the present time, even in cases of scarlet fever.

The microscopic study also brought out other lesions of interest, which had not been apparent in the gross. There was a very severe and acute myocarditis, which has been described in sulfonamide reactions by French and Weller,² of Ann Arbor, but which we have never seen here. This was extensive enough so that I think the sudden terminal exitus was in part due to that as well as to the uremia. There was also an extensive change in the pancreas, but it is a little less certain whether one can blame it on the drug; very possibly it was of entirely different origin. A number of pancreatic ducts showed squamous-cell metaplasia, many of them blocked with inspissated casts. There was slight dilatation of the acini, as well as a moderate inflammatory infiltration and a few places where the islands of Langerhans were found imbedded in fat tissue without any surrounding acinar tissue, suggesting a significant degree of pancreatic atrophy; the picture is reminiscent of the very early stage of so-called "cystic disease of the pancreas" seen in small children.

Dr. Maisel, have you anything to add?

DR. BERNARD I. MAISEL: The only thing I should like to say is in answer to Dr. Richardson's comment that the blood level was 2.2 mg. per 100 cc. almost a week after the drug had been stopped. We have found that to be so when the kidneys are damaged. In other words, a diseased kidney often will not excrete the sulfonamide drugs; hence, if a patient who is given the usual dose of the sulfonamides develops a high blood level, one must suspect renal impairment and be extremely careful in continuing the drug.

DR. MALLORY: Dr. Nathaniel Faxon once remarked that he thought seriously of having tattooed upon his chest, "Do not give me any transfusions." I sometimes think it would be a good idea if one said, "Do not give me sulfonamide for any nonlethal complaint."

DR. GEORGE W. HOLMES: There is some evidence of lung pathology by x-ray. Did you find anything?

DR. MALLORY: There were pulmonary edema and epithelization of the alveoli, which suggest that the edema had been present for some time. This is not, however, the type of pulmonary edema that Dr. Schatzki has observed in nephritis.

A PHYSICIAN: Was the brain examined?

DR. MAISEL: No.

DR. WILLIAM B. BREED: This case brings up the question of the duty of the profession in educating or re-educating the public. I spend many of my waking hours preventing the promiscuous use of sulfonamides in patients because of the pressure brought to bear by friends, their families and themselves. We can do a great service if we, as physicians, will take this opportunity to continue the education of the public with respect to the use of these drugs, counteracting the influence of newspaper and magazine articles.

DR. RICHARDSON: We might start with the staff.

DR. BREED: That is one of the purposes of the above remarks.

DR. WILLIAM H. BECKMAN: Was there any evidence of periarteritis?

DR. MALLORY: No. There were a few cells around one coronary artery, but I do not think that makes it periarteritis.

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CASE 29212

PRESENTATION OF CASE

A fifty-eight-year-old housewife entered the hospital because of headaches of two weeks' duration.

Two weeks prior to admission, soon after a hearty supper, the patient suddenly became warm, dizzy and nauseated. She tried to vomit but could not. Approximately half an hour later she developed a sharp throbbing occipital headache and perspired profusely. She took bicarbonate of

soda and promptly vomited, but without much relief. Because she felt weak and faint she went to bed. However, at no time did she lose consciousness. Her physician found the systolic blood pressure to be 185, and gave her codeine sulfate and "another tablet which lowered the blood pressure." During the two weeks prior to admission she had three similar attacks each lasting about half an hour, but these were not so severe and responded readily to "hypodermic injections." No auras accompanied these attacks, nor was a neurologic residual noticed afterward. There had been slight diminution of visual activity during the year prior to admission. The patient had no genitourinary symptoms.

The family history was noncontributory.

For more than twenty years the patient had had dizzy spells following "bilious attacks" from overeating. These occurred about every two years, were followed by nausea and vomiting and then spontaneously cleared. There had been no fever, chills or jaundice during these attacks. The patient had been married for thirty-six years, but had never been pregnant. A hysterectomy and bilateral salpingo-oophorectomy were performed eighteen years before admission for "fibroids of the uterus."

Physical examination disclosed a thin, nervous woman who seemed quite well. The heart was slightly enlarged to the left, and there was a short early blowing systolic murmur best heard in the aortic area. The lungs and abdomen were normal. A neurologic examination was not remarkable. The visual fields were normal.

The blood pressure was 140 systolic, 88 diastolic. The temperature, pulse and respirations were normal.

The examination of the blood revealed a red-cell count of 4,700,000, with a hemoglobin of 14.0 gm. and a white-cell count of 8800 with 58 per cent neutrophils. In eleven examinations of the urine the specific gravity varied from 1.010 to 1.018, was acid in reaction and gave a + test for albumin on two occasions; six times the sediment contained a few red cells, white cells and epithelial cells per high-power field. A blood Hinton test was negative. The nonprotein nitrogen was 32 mg. per 100 cc., and the blood sugar 92 mg. A phenolsulfonephthalein test showed 25 per cent excretion of the dye in the first fifteen minutes, and 60 per cent in two hours. The basal metabolic rate was +1 per cent. An electrocardiogram showed a normal rhythm, with a rate of 70. T₁ and T₂ were upright and of good amplitude, and T₃ was slightly inverted. There was a slight tendency to left-axis deviation. The P waves and the PR intervals were normal. An electroenceph-

alogram was said to have been consistent with a mild diffuse process resulting from hypertensive attacks.

On the third hospital day, at 9:00 p.m., a cold-pressor test was performed. The initial blood pressure was 115 systolic, 68 diastolic. After the left hand had been in ice water approximately forty-five seconds, the patient complained of excruciating bilateral occipital headache, radiating forward to the temples and to the forehead, and a severe pounding pain developed in these areas. This attack was identical with the spontaneous attacks. Five minutes later the blood pressure rose to 180 systolic, 110 diastolic. There was no palpitation, precordial pain, change in skin color, sweating, dizziness, nausea, blurring of vision, tinnitus or deafness. Within three minutes after the hand was removed from the water, the headache slowly began to disappear. However, the blood pressure continued elevated. There was little change in blood pressure when the head of the bed was elevated 15° or when the patient sat up. At the conclusion of the test, with the patient lying flat, the blood pressure was 178 systolic, 105 diastolic. At 10:30 p.m. the pressure was 134 systolic, 80 diastolic. Three hours later the patient had a typical attack, which began while she was in bed. Luminal had been administered approximately three hours prior to the attack. When seen, the patient was very restless, perspired freely, rolled about in bed complaining of a severe occipital headache and begged for sedation. The blood pressure was 174 systolic, 114 diastolic, and 170 systolic, 112 diastolic, in the right and left arms respectively with the patient flat in bed and the manometer level with the right arm. The pupils were small and did not react to light. There was questionable evidence of weakness of the left seventh cranial nerve. Ten minutes after morphine sedation the headache was relieved and the patient seemed quite comfortable.

An operation was performed on the eleventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT E. GLENDY: In summary, this history is that of a woman in her sixth decade suffering from peculiar spells attended by a variety of symptoms and signs, among which was paroxysmal hypertension, and, who, after ten days of hospital observation, was thought to have a condition requiring operation. The problems are, Why did she need an operation and what was found at operation?

The past history is not remarkable except for bouts of indigestion attributed to overeating, which

may very well have been due to this cause. These episodes went back over a period of twenty years, at intervals of about two years, and, at least in the patient's mind, bore no relation to the "spells" that finally brought her to the hospital. Whether the bilious spells were related to the present illness makes little difference in so far as the differential diagnosis is concerned, for we have no data concerning the blood pressure during the attacks of indigestion, and can only speculate about it. She was never pregnant, but I have no way of telling from the history whether this was by accident or design or for other reasons.

The attacks that began to occur two weeks prior to admission seem more complex and more incapacitating than anything that preceded them. They were characterized by flushing, dizziness and nausea, and later a throbbing occipital headache, profuse sweating, weakness and faintness. Induced vomiting did not afford much relief. One might encounter this set of symptoms under all sorts of circumstances, but the fact that they were attended by an elevated blood pressure should make one suspicious of a hypertensive crisis, even in the absence of the neurologic manifestations that so often occur in such crises. Subsequent observations failed to show a persistent hypertension. This is against hypertensive crisis as one usually thinks of it in individuals with well-advanced, often malignant hypertensive cardiovascular disease, when it is preceded by prodromes of malaise, headache, vomiting, apathy and paresthesias. There seems little doubt, however, that the attacks were on the basis of a sudden marked, paroxysmal rise in blood pressure without prodromal symptoms, and when the pressure returned to lower levels, the symptoms subsided. The only definite precipitating factor up to the time of admission seems to have been overeating; at least, other circumstances are not mentioned.

She is described on physical examination as thin and nervous, but seemed quite well. These statements are somewhat contradictory, but one can surmise from them that she was not of hypertensive habitus, that she was not cachectic and that she did not possess any of the bizarre physical manifestations of a glandular disorder. There was some cardiac enlargement, which I presume could be the result of even paroxysmal hypertension. If this presumption is correct, the systolic murmur heard in the aortic area might be explained on the basis of dilatation of the aortic ring. Furthermore, if the cardiac enlargement was the result of paroxysmal hypertension, this would indicate a condition of long-standing, slow progression, with acceleration during the few weeks before admission. There is certainly no con-

clusive evidence of a valvular lesion, such as aortic stenosis, but since this condition is sometimes attended by vertigo and fainting, one might consider it remotely as a factor in her symptoms and as a cause of the cardiac enlargement. I believe, however, that it can be discarded. No mention of the condition of the retinal arteries during or between attacks is made, so I shall assume that they were not remarkable.

"The pupils were small and did not react to light." I do not know how to interpret that finding. No mention is made of the pupils on initial examination. I presume that she had not had an opiate, although that is a possibility since she did get morphine later.

Do you know whether any ophthalmoscopic examination was made?

DR. REGINALD H. SMITHWICK: The pupils were normal.

DR. GLENDY: During the attack?

DR. SMITHWICK: No one looked during the attack. At the time of admission they were perfectly normal.

I happened to see this woman in an attack. She had several while in the hospital. One of these occurred when I suggested that she be operated on,—just as one occurred when her hand was put in ice water,—and it was a rather alarming attack. She was extremely nervous, had excruciating occipital pain, was restless and dizzy, with a definite elevation of the pulse rate, slight tremor, a feeling of constriction in the chest and a sense of impending disaster,—she thought that she was going to die.—and believed that she was going to have a severe nosebleed.

DR. GLENDY: That certainly gives a more complete picture of the attacks.

The initial blood-pressure reading of (140 systolic, 88 diastolic) is certainly within normal limits for the patient's age. Subsequent readings while at rest were even lower (115 systolic, 68 diastolic).

I can gather no light on the problem from the laboratory procedures. Two of eleven urines showed a + test for albumin, and in half the urine specimens there were a few red and white cells; but all tests of kidney function were normal. There was nothing clinically or by laboratory test to indicate disturbance of the basal or carbohydrate metabolism.

The results of the cold-pressor test were striking, demonstrating a sharp reactivity of the mechanism regulating the blood pressure. The response, however, was out of all proportion to what one might expect, even in patients with known persistent hypertension. I consider the cold as just another factor that reflexly precipitated the par-

oxysm of hypertension and its attendant symptoms.

There is only one condition I know of that might produce this clinical picture. It was referred to in 1934 by Belt and Powell¹ as the "suprarenal sympathetic syndrome" and occurs in patients with tumors arising from the chromaffin tissue. I believe this patient had such a tumor. Having chosen chromaffin-cell tumor (also called paraganglioma, pheochromocytoma and chromaffinoma) as the most likely diagnosis, there is little I can say against it. Two prominent features that have been present in most of the reported cases are precordial oppression and severe palpitation. This patient had no palpitation, but Dr. Smithwick did note that she experienced a sense of constriction in the chest. Loss of consciousness and convulsions do occur but are infrequent. The blood pressure is usually normal between attacks, as in this case, or may be persistently elevated, making the differential diagnosis between paraganglioma and late essential or malignant hypertension difficult. Palmer and Castleman² reported a case in which the patient had paroxysms of hypertension but also persistent hypertension between attacks. The mechanism involved in these attacks is thought to be the intermittent discharge of adrenaline into the blood stream from the site of the tumor. Crystalline adrenaline has been recovered from the tumors, which lends support to this idea, but on account of the extremely low concentrations of adrenaline in the blood even during attacks, it has not been possible, so far as I know, to isolate it from the blood stream. Is that a true statement, Dr. Albright?

DR. FULLER ALBRIGHT: Yes.

DR. GLENDY: The tumor may be located in either or both adrenal glands, or anywhere along the sympathetic chain where chromaffin cells exist, that is, as far down as the bifurcation of the aorta. Trauma or manipulation of the abdomen either in examination or in surgery may precipitate an attack. There is no evidence from the physical examination that any abdominal tumor exists in this case. In cases that have been reported, the use of contrast pyelography and pneumoperitoneum has been of value in localizing the adrenal tumors. Were any such studies done here?

DR. TRACY B. MALLORY: No.

DR. GLENDY: If I am forced to guess where the tumor lies, the following locations are most frequent in the order mentioned: right adrenal gland, left adrenal gland, bilaterally in the adrenal glands and, finally, the extramedullary chromaffin tissue, such as the sympathetic ganglions and the

carotid body. I shall guess on the law of averages that it is in the right adrenal gland.

The condition occurs predominantly in females in a ratio of 3:1, and most often in the third, fourth and fifth decades, but 1 case has been reported in an infant. Some of the reported cases have been confused with anxiety attacks or hysteria. Although there often is a marked rise in blood pressure in anxiety states, it is not of the magnitude encountered with the suprarenal sympathetic syndrome associated with a paraganglioma. Hyperthyroidism has also been confused with this syndrome, but the enlarged gland, other physical signs and elevated metabolic determinations usually make the distinction clear. The presence of hyperglycemia and glycosuria, which are sometimes found in cases of paraganglioma, has raised the question of diabetes mellitus, but the absence of a fundamental and continued disorder of sugar metabolism rules out this disease. Intermitent hypertension in association with cortical adrenal tumors has also been observed by Fishberg,³ but his cases were accompanied by clinical manifestations of hirsutism and virilism not present in this case.

DR MALLORY: Will you tell us your findings, Dr Smithwick?

DR SMITHWICK: Paroxysmal hypertension is a rare disorder. In our experience here in the last ten years in studying hypertension of one sort or another we have seen only a very few cases. Up to within a year, a total of 116 cases associated with adrenal medullary tumors was reported in the literature.⁴ The great majority of these tumors were discovered at autopsy. In addition there have been a few cases, I do not know how many, in which the patients had paroxysmal hypertension and at operation no adrenal tumors were found. As Dr Glendy has said, the tumors occur most commonly in the adrenal glands or in their vicinity, but occasionally they are found in other parts of the body, and the fact that most of the operations that have been done have been limited to exploration of the adrenal glands does not prove that a paraganglioma might not have existed elsewhere. However, there are occasional cases of paroxysmal hypertension of a neurogenic type not associated with adrenal tumors, and that is what this particular case proved to be.

The patient was explored carefully from the low lumbar to the midthoracic level on both sides by the retroperitoneal extrapleural approach, and both adrenal glands were found to be normal. Biopsy specimens were taken from both adrenal glands and from both kidneys. The main renal arteries were normal.

Because of the similarity between the patient's reflex blood pressure response to emotion and cold and those of the usual patient with essential hypertension, the chief difference being the duration of the attacks, it seemed best, in the absence of a pheochromocytoma, to denervate the splanchnic bed. This was done, and the attacks have not recurred in the year and a quarter since operation. It therefore appears that this patient had paroxysmal hypertension of neurogenic origin.

CLINICAL DIAGNOSIS

Paroxysmal hypertension

DR GLENDY'S DIAGNOSIS

Chromaffin cell tumor (paraganglioma), probably of right adrenal gland

ANATOMICAL DIAGNOSIS

(Paroxysmal hypertension of neurogenic origin)

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN: The adrenal and renal biopsies were normal. Careful examination of the renal arterioles showed no vascular disease. This woman falls in the group of hypertensive patients recently reported⁵ in which study of the renal biopsy specimens, taken when sympathectomy was performed, showed little or no arteriolar disease, which is evidence in favor of the theory that the hypertensive state antedates the renal vascular disease.

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CONCENTRATED HUMAN SERUM ALBUMIN

EVERY physician, no matter what his interest or specialty, should know how to treat certain medical emergencies. One of the most important of these is shock, an everyday occurrence in the armed forces overseas, but a sufficiently frequent condition in civilian practice to demand preparedness on the part of every practitioner. The necessity for this is emphasized by the possibility of air raids and the actuality of disasters like the Cocoanut Grove fire. Recent improvements in the methods of preparing and preserving blood plasma and the development of blood banks have placed potent weapons against shock in the hands of the medical

profession. In order to use these weapons intelligently, it is necessary to understand the differences between the various forms of preserved plasma and its derivatives. Much valuable practical information about the available blood substitutes appears in a paper by Newhouser and Lozner, published elsewhere in this issue of the *Journal*. The authors speak authoritatively from their experience in the Blood Research Division of the National Naval Medical Center, and include information about concentrated human serum albumin, the latest addition to the group of blood replacement fluids used in the Army and Navy.

All previous methods of plasma preservation have been aimed at keeping the plasma intact. The work of Cohn¹ and his colleagues has introduced a radically new idea into this field, namely, the separation of plasma into its active components and their use in a relatively pure state for specific purposes. Concentrated human serum albumin, one of the accepted remedies for the treatment of shock, represents the fulfillment of this idea, and is an example of how a practical achievement can arise from scientific work carried out on a fundamental level.

Concentrated human serum albumin was developed for the armed services as a result of the need in certain situations for a blood substitute that would take up a minimum of space and be ready for use with a minimum of preparation. Although dried plasma has become the basic therapeutic agent in the Army and Navy, it requires a bulky package and a certain amount of time is necessary to reconstitute the plasma for use. Albumin, as issued to the armed forces,² is in solution, ready for instant injection, and is concentrated to such an extent that it occupies little space.

Albumin has certain properties that make this possible. It is not only the most stable protein of the plasma but also the most soluble; hence it can be concentrated to form solutions that are capable of withstanding considerable extremes of temperature without deterioration. It has been used sufficiently to indicate that, when properly prepared, reactions almost never occur. It is well

known that the colloidal osmotic pressure of the blood plasma is due to its proteins and that, of these proteins, albumin is responsible for at least 80 per cent of the colloidal osmotic pressure, although it constitutes only slightly over half the total protein. Hence, it is the most effective component of the plasma in restoring the depleted plasma volume characteristic of surgical shock.

Proof of the practical usefulness of concentrated albumin has been supplied in a study by Woodruff and Gibson,³ in which it was found to be an effective agent in the treatment of traumatic shock in civilian hospitals in the United States. That albumin is an exceedingly safe remedy is the inevitable conclusion from the paucity of reactions observed. That it may lead to trouble if used in excessive dosage without an understanding of its particular properties is reasonable, and is emphasized by Newhouser and Lozner. However, the precautions to be observed in its use are mainly those that apply to the use of plasma itself. If huge doses of albumin are used, three difficulties may arise. First, the patient may develop a deficiency of the globulin components of the plasma, among which are to be found the antibodies, which assist in the defense against infection, and prothrombin and fibrinogen, which are essential constituents of the blood-clotting mechanism. In the second place, the osmotic potency of albumin is so high that the circulation may be overloaded. This is hardly a danger in the treatment of shock, in which the patient is suffering from a deficiency of circulating blood. The third possible difficulty results from the fact that albumin is put up in concentrated solution. This means that, as the concentrated protein solution is injected into the blood stream, fluid is drawn into the circulation from the patient's tissues. If the patient is extremely dehydrated, with the interstitial fluid reserves markedly depleted, concentrated albumin can scarcely be expected to produce as good results as in a well hydrated one, and treatment in such patients should be supplemented with oral or parenteral fluids.

It should be emphasized that, just as plasma is not a "blood substitute" but a therapeutic agent in its own right, so albumin is not just a "plasma substitute" but a therapeutic agent with new properties and specific indications. Concentrated plasma or serum differs from it, because the concentration of the globulins leads to high viscosity, whereas the viscosity of the official 25 per cent albumin solution is no greater than that of whole blood, as Newhouser and Lozner point out. The concentration of electrolytes is much higher in concentrated plasma than in concentrated albumin.

The effectiveness of this new remedy under military conditions remains to be tested on the field of battle. There is ample proof from preliminary trials in civilian hospitals that concentrated human serum albumin is not only a safe but an exceedingly valuable agent for the emergency treatment of shock because of its instant availability and its rapid action in increasing the blood volume. The concept of utilizing one component of plasma for a specific indication may have many other fruitful applications to the treatment of disease.

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THE ROCKFELLER FOUNDATION REPORTS

GEARING its work to the war emergency, yet maintaining its long range viewpoint, the Rockefeller Foundation in 1942 appropriated \$8,227,867, distributed for the most part in the major fields of public health, the medical, natural and social sciences, the humanities and reconstruction in China. The two largest items were \$2,700,000 for public health and \$1,434,000 for the medical sciences. Seven members of the staff of the International Health Division were absorbed into the armed forces to deal with such specialized problems as malaria and typhus, and twelve are serving

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cede with the lowering of the knees The diagonal conjugate now measures

- F 111 cm (a difference of 9 mm)
- B 116 cm (a difference of 13 mm)
- S 110 cm (a difference of 8 mm)

R W B

WAR ACTIVITIES

INDUSTRIAL HEALTH

The following recommendations concerning a control program for venereal disease in industry have recently been made by the Advisory Committee on the Control of Venereal Diseases, United States Department of Public Health

In order to assemble current authoritative information and to formulate basic principles applicable to a program of venereal-disease control in industry, the Surgeon General has appointed an advisory committee to the United States Public Health Service. This committee has outlined the objectives of such a program as follows

A Medical and Public Health

(1) To find and refer for proper medical management all cases of venereal diseases among workers in industry

(2) To establish equitable policies for the employment of applicants and continuation of services of employees who have venereal diseases

(3) To co-ordinate the community and industrial venereal disease control programs

B Employee

(1) To improve the physical condition of employees

(2) To reduce the number of workdays lost through illness or injury

(3) To provide job placement

(4) To prolong and increase the earning power of employees

C Employer

(1) To reduce compensation costs

(2) To lessen work interruptions and labor turnover

(3) To enhance production by increasing the efficiency of workers

(4) To minimize personnel problems

In order to assure agreement on all phases of fundamental policy, the committee recommends that certain agencies be consulted in carrying out this program: the labor department, industrial commission or similar department of state government, the appropriate committee of the state medical society, the association representing employers, the labor organizations and the appropriate voluntary health and welfare associations

Responsibility for the administration of the program should be shared by the industrial hygiene and venereal disease divisions of the state health department. The program should not be inaugurated without a complete educational program. The employee should be convinced that adequate treatment protects both his health and his ability to earn a living, and the employer that not all cases of venereal disease are infectious, through an educational program before venereal-disease control measures are introduced

In order that the control program may be effective, pre-employment examinations should be mandatory for

all workers. Laboratory tests for syphilis and gonorrhea should be made a part of the periodic, re-employment or return from illness physical examinations that are the policy of the industry. The interval between examinations should under no circumstances be more than three years

It is of utmost importance that the results of the medical examination be considered confidential between the worker and the medical staff. Information should be furnished to others only with the consent of the individual concerned or, failing this, on legal advice. The medical staff should make proper recommendations to the management concerning the physical fitness of the employee for work. When the usual clinical record is kept in an open file, venereal-disease forms should be filed in the medical departments for the use of the medical staff only

There is no reason for denying employment to an applicant or for discharging an employee because an examination has revealed evidence of syphilis or gonorrhea provided

(1) That the employee agrees to place himself under competent medical management

(2) That if the disease is in the infectious stage employment should be delayed or interrupted until such time as a noninfectious state is established through treatment and open lesions are healed

(3) That when syphilis exists in a latent stage employment should not be delayed or interrupted

(4) That employment may be deferred or denied when the individual is an industrial hazard

(5) That occupational readjustments of employees be made of individuals developing disabling manifestations

(6) That workers with syphilis in any of its stages be excluded from areas where there is exposure to chemicals that may produce toxic reactions and that those having cardiovascular syphilis or neurosyphilis should not be exposed to physiologic stresses

(7) That workers with gonorrhea should be allowed to work only under special medical observation during the administration of sulfonamide drugs

The applicant or the employee whose examination reveals evidence of a venereal disease should be called to the industrial physician's office for a conference. He should be instructed concerning the nature of the disease in order that he may co-operate intelligently with the requirements of the program. He should be referred to a reputable source for medical attention and be furnished with a letter directed to his physician stating the results of the examination and what is expected of the employee in regularity of treatment if he is to be employed. The industrial physician should receive a record of treatment at about monthly intervals. The names of persons who have neglected or refused treatment should be turned over to the health department for appropriate action in bringing them to treatment

The plant physician making a tentative diagnosis of communicable syphilis or gonorrhea should without delay acquaint the appropriate health authority with the facts

CORRESPONDENCE

OLD MEDICAL DICTIONARIES WANTED

To the Editor Although the chief function of the Citizens Committee for the Army and Navy Incorporated

is to furnish dayrooms in camps and to supply recreational equipment to the Army, Navy and Coast Guard, we also strive to fill unusual requests received from special-service officers. In many cases, the materials or services requested are theoretically covered by Army and Navy appropriations. As a practical matter, red tape and endless delays substantially negate the right of various units to benefit from governmental appropriations.

Typical examples are the urgent requests that have been made to us from a number of units for medical dictionaries. We are advised that many trainees are wholly unfamiliar with the medical terms that they are obliged to use in their training. This puts an additional burden on their instructors.

This committee has appealed to various medical libraries and schools without success. If you would generously grant us space in your columns to publish this letter, we have great hopes that some of your medical readers will be willing to send to Committee Headquarters, 13 Commonwealth Avenue, Boston, any medical dictionaries, no matter how old or how dilapidated, that they can spare. If the dictionaries cannot be sent or delivered to Committee Headquarters, arrangements can probably be made by telephone (COMMONwealth 6810) to have them picked up.

JOHN HEARD, *Vice-President*
The Citizens Committee for the Army
and Navy, Incorporated

13 Commonwealth Avenue
Boston

WILLIAM ALLAN

To the Editor: It is particularly appropriate to memorialize in the *Journal* the life and works of William Allan of Charlotte, North Carolina, who recently died of pneumonia in Winston-Salem, whither he had gone not long ago to take a new post at the Bowman-Gray Medical School in the field of inheritance of diseases in which he was a pioneer.

Dr. Allan was not only one of the leading physicians and internists in the United States and an authority and intensive worker in his chosen special field, but he had become known personally, through his associations during World War I, to a group of New Englanders who made up the large portion of Base Hospital Unit No. 6, stationed at Talence near Bordeaux, France, from 1917 to 1919. As the chief internist of Unit O attached to the hospital in the winter of 1918, he quickly endeared himself to the Yankees in Talence and also quickly demonstrated his great ability both in the theory and in the practice of medicine.

Many of us in New England, both in and out of that old hospital unit, have continued to keep in touch with Bill Allan ever since. He was a man whom all his friends loved dearly. One of the interesting circumstances of his life was that his father was one of Stonewall Jackson's most important officers in the War between the States. His grandfather founded and taught at the Military Institute of Virginia.

Medicine, and especially the new field of hereditary medicine, will miss Dr. Allan, but his friends and associates will miss him still more.

PAUL D. WHITE

Massachusetts General Hospital
Boston

BOOK REVIEW

Spontaneous and Experimental Leukæmia in Animals, By Julius Engelbreth-Holm, M.D., director of the Cancer Research Laboratory, Danish Anti-Cancer League, and chief pathologist of the Finsen Institute and Radium Station, Copenhagen. 8°, cloth, 245 pp., with 44 illustrations and 3 tables. Edinburgh: Oliver and Boyd, 1942. 15 shillings.

This book, which was written at the behest of the famous Lady Tata Memorial Trust by an internationally known investigator with a broad clinical experience and viewpoint, gathers up the many diverse and often tangled threads of leukemia as seen both in spontaneous and experimental animal leukemia and in man. It thus fills a long-felt need for both the interested clinician and the investigator.

Of the spontaneous and transmissible leukemias in fowl and mammals, the lymphogenous type is by far the most frequent, and in fowl appears to have a seasonal variation. Plasma-cell leukemia and its related multiple myelomatosis is unknown in animals. Although mouse leukemia can be transmitted by a single cell, but never by a cell-free filtrate, there are inferential facts that a virus etiology may be a factor. In fowl, myelogenous—but not lymphogenous—leukemia and erythroleukemia can be produced by a filterable virus. The spontaneous remission and recovery of fowl leukemia are discussed. A virus has been found in fowl sarcomas of the same histologic type as mammalian sarcomas.

The role of heredity and its significance in spontaneous and transmitted animal leukemias are discussed, together with the present knowledge relative to experimentally produced leukemias in fowl and mammals by carcinogenic agents, x-ray irradiation and estrogenic substances.

Of greatest interest to clinicians is the final chapter, which deals with the nature of animal leukemias and their relation to human types. All the evidence points to the conclusion that leukemia is a neoplastic proliferation. Although, in contrast to other neoplasms, leukemia is generalized from the start, this probably depends on the peculiarity of the blood-forming tissues themselves, which are normally scattered throughout the body and not situated in a simple locus. Furthermore, they produce cells that lack the ability to form cohesive tissue and thus, in proliferating, produce a generalized disease, usually without nodal metastases. The many relations between such diseases are pointed out, for example those between lymphosarcoma and lymphatic leukemia. Thus the peculiarities that distinguish leukemia from other tumors can be readily explained as consequences of the special features normally characterizing the hematopoietic tissues. Direct evidence concerning the neoplastic nature of leukemia has been developed by the author and Furst, who worked with mixed leukemia-sarcoma strains. As Engelbreth-Holm states, leukemia research has become a link in general tumor research, and results in this field will presumably be of value in the understanding of the others. He adds, "There can be no legitimate grounds for doubt that leukemia in animals, especially in mice, is the same disease as that in man . . . with the solution of the problem of human leukemia as the final goal. . . ."

This book, which presents an authoritative analysis of all the scattered notions and studies of animal and human leukemia, is a "must" on the list of those interested in tumors and blood diseases.

(Notices on page viii)

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THE UNIVERSALITY OF A SPECIALTY²⁴

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BOSTON

HAS been said that a specialist is one who knows more and more about less and less. It not but might have been said as well that a general surgeon, medical man or practitioner is one who knows less and less about more and more. Though neither of these definitions is to be taken literally, there is enough truth in them to warrant an attempt to estimate just how special a specialty is and how general a practitioner or surgeon should be. I can speak only about one specialty, — neurosurgery, — but I believe that any conclusions concerning the universality of that specialty will be found to apply with only minor modifications to all others.

Neurological surgery at its birth was the surgery of tumors of the central nervous system. Its origin was unquestionably Harvey Cushing, and among its ancestors are found such men as Abernethy, Von Bergmann, Kocher, Kroenlein, Koenig, Heller, Doyen, Horsley and others too numerous to mention and doubtless of equal importance. Its early near relatives — uncles, perhaps — were Elsberg, de Martel and Frazier. The latter with Cushing took the first step toward broadening the scope of this specialty by demonstrating a practical method of dealing with pain in certain tumors. The added breadth was not great, however, and neurosurgery remained for years, and indeed is still thought by many to be, pre-eminently the surgery of tumors of the nervous system.

Because they were engaged in pioneering, and because of lack of faith in the explorers as well as lack of intelligent interest on the part of other specialists, the first neurosurgeons had to practice a great deal more than surgery. First of all, they had to be neurologists. The differential diagnosis of an intracranial tumor was not then the relatively simple procedure it is today, complicated though this may be. Nor was the existence

of many of the strictly neurologic entities as possible causes of tumorlike symptoms known or suspected by the general practitioners and surgeons who first saw such patients at the start of the twentieth century. Ophthalmoscopy was handicapped by the crude method of obtaining light for the examination. It was practiced only by "eye men," to many of whom a choked disk meant optic neuritis and nothing else. The study of the pathology of the central nervous system, except for the grossest kind, was in its infancy, and a knowledge of the histology of cerebral neoplasms did not exist. Finally, along with any therapy of these tumors went the need for continual revision of what was then known about the physiology of the central nervous system. The burden of all this lay directly on the shoulders of the neurosurgeon. If he failed or refused to carry it, his diagnosis went wrong and his operations were performed too late or in the wrong place, or for conditions that only simulated tumors. Lack of adequate post-mortem studies of the brain led him astray in as yet unoperated living patients, and the apparently contradictory data thus obtained had to be rationalized in the physiologic laboratory. The early neurosurgeons, then, in addition to being highly skilled technicians and competent general surgeons, had also to be their own medical man, ophthalmologist, neurologist, pathologist and physiologist. This made a tremendous demand on their time and energy and constrained them to limit their interest to those patients whose study along such broad lines would most repay them. Obviously these conditions were best met by relatively circumscribed lesions such as tumors, and by the physiologically experimental kind of surgery that had to be practiced for the relief of pain in isolated areas of the body. For all these various reasons, therefore, neurosurgery at its start and until the beginning of World War I was practiced almost exclusively in the treatment of tu-

²⁴ Before the annual meeting of the Tufts College Medical School, June 4, 1942, I was elected to the Alpha Omega Alpha, Boston Chapter, 1942.
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mors of the central nervous system and to the relief of pain.

What of the general men at this time? By general men I mean the general surgeons, the general medical men and the general practitioners. This was the "golden age of surgery." Asepsis had replaced antisepsis, and a knowledge of physiology was supplementing the astounding anatomical proficiency that was then the pride of the profession. The abdominal cavity could now be freely opened and the bowel dealt with without contamination of the peritoneum. Surgery of the prostate and bladder, the thyroid gland and malignant disease was making rapid strides. Patients were finally learning that going to the hospital was not a method of committing suicide and that surgical procedures when carried out in the home, although more convenient for visiting friends and relatives, were disrupting to members of the immediate family and dangerous to themselves. In medicine, the shotgun prescription was coming to be discarded, and not long afterward a period of therapeutic nihilism developed. Such radical departures as the writing of prescriptions in legible English instead of in Latin was another symptom of medical realism. Medicine, too, began to be less anatomic and more physiologic. The value of the hospital also became apparent in nonoperative patients, and the physician came to rely more and more on the consultative opinions of his surgical colleagues, and vice versa. The general practitioner, being almost always without hospital facilities, had to be both surgeon and medical man. He learned about the progress being made in his profession secondhand and developed a tremendous initiative, inventiveness and physical stamina, as well as a sense of his own enforced intellectual inadequacy. With the change of the public's point of view toward hospitals, he was in the forefront of the move to build more of them and to make more use of those that were already available. In this way his work was lightened and done better. Furthermore, he soon found that the local hospital was a magnet that drew surgeons and medical men from the large centers so that he could "tap their brains," profit by their demonstrations, and bring himself more nearly up to date, while giving better care to as many patients as he had always had, or even more.

All these general men, as the numbers and efficiency of hospitals grew, found that because of their availability in emergencies they must be prepared to deal more and more with trauma. In its very nature this meant diagnosing and caring for injuries to the bony skeleton and its contained organs, the brain and spinal cord, the body cav-

ities and their contents, and the coverings of the extremities, such as the muscles, blood vessels and peripheral nerves. Thus a part of what should have been neurosurgery was kept separate from that specialty, partly because of the preoccupation of the neurosurgeon with tumors and pain, and partly because the public by its use of the hospitals forced the general man to assume responsibility for the diagnosis and care of the results of injuries to the central and peripheral nervous system.

These and other forces gradually made general specialists of the surgeon and the general practitioner, and forced them to learn how to deal with any surgical problem that arose. My father, John C. Munro, for example, was most interested in the stomach and duodenum and did most of his significant work with them. His experience was sufficiently great, however, so that in 1902 he wrote a paper on subdural hematomas, in which he advocated what is now recognized as the best modern therapy of these clots, and in 1899 and 1904 others on the efficacy of laminectomy in spinal injuries. He also held and published strong views on the therapy of malignant disease, surgical infections of the kidneys and portal infections associated with appendectomy. In addition, he worked out and first published the principles underlying the modern method of ligating the ductus arteriosus and in 1907 reported a case of attempted ligation of the abdominal aorta for aneurysm. A. J. Ochsner did a hysterectomy, amputated a lobe of the liver, removed a toxic goiter, dissected a neck, and avulsed the sensory root of a gasserian ganglion with equal nonchalance and, except for the latter, with a skill and dexterity that can scarcely be matched today. Samuel J. Mixter, father of one of the distinguished neurosurgeons of today, and Dr. Fred B. Lund, the present senior surgeon of Boston, had the same versatility; the ability of Maurice Richardson and the Mayo brothers in every surgical field is well known.

Such, then, was the approximate situation when World War I broke out in 1914. Surgeons were general surgical specialists, and were expected to do, and did do, any kind of surgery in any part of the body. Such specialists as the neurosurgeons with their tumors, the orthopedists with their tuberculous spines and flat feet, the nose-and-throat men with their mastoids and the dentists with their tooth extractions were regarded for the most part as necessary evils who must be countenanced because of their occasional invaluable aid in a problem that the general surgeons or practitioners were not able to solve alone. As was pointed out at the start, the specialist of that era was

indeed a man who knew more and more about less and less

After the war it soon became generally apparent that the accumulation of knowledge about the effect of trauma on the body was far exceeding the ability of the general surgeon to absorb it all. Both he and the specialist had to revise their ideas. In neurosurgery intimate knowledge of how to deal with tumors of the central nervous system had been of little importance in the hospitals of France, whereas a more detailed and practical knowledge of how to handle the effects of trauma on these same anatomic structures was a crying need. By the same token, surgery of the chest and orthopedic and maxillofacial surgery demanded the full attention of those who had previously indulged in these fields as a hobby only, and by the time the armistice was signed the specialist as such had ceased to be a necessary evil and was an indispensable member of the surgical profession in the mind of the public. Financial stringency, professional jealousy and the dislocations in civilian practice that arose out of relocating ex Army doctors, as well as the postwar neurosis that affected to varying degrees almost all who were intimately associated with the armed forces, led to the temporary development, however, of what might be called an antispecialist reaction in the profession itself. This was most noticeable among the staffs of large municipal hospitals and the ranks of the general practitioners. Rather than countenance what was believed by many to be, and what latterly in some cases actually was an infringement of their surgical rights, these surgeons leaned over backward in their zeal they attempted to carry on the prewar tradition of being general specialists, and to deal with certain surgical problems that were beyond their mental and technical abilities. It was at this time—perhaps twenty to twenty-five years ago—that the antithesis of the definition of a specialist was most aptly applicable to these general surgeons and the few remaining general practitioners. They were indeed men who knew less and less about more and more.

The Army and Navy, just as they do today, also encouraged general specialism. World War I did not last long enough for them to learn permanently the lesson that armed combat forced them to the cognizance of just before the armistice. Despite the then proved value of specialist consultants and hospitals staffed for and limited to the care of one specialty, it is now apparent that that knowledge has been thrown aside. The old system whereby the officer-of-the-day who though trained as an allergist or ophthalmologist must nevertheless operate on any patient with an

acute appendix who is admitted to the hospital at night during his tour of duty, is still in use in this present emergency. To be sure, one general surgeon in every large service hospital may be assigned as a specialist or vice versa, but the fundamental concept in both the Army and Navy men today apparently is still that which visualizes the general surgeon as a general specialist. The armed services appear to ignore the fact that the public has learned by experience that this is a fallacy.

In so far as neurosurgery was concerned, the group with such ideas was aided and abetted by most of the specialists in this field, who for many years after the close of the war, and despite the experience they had had therein, still regarded neurosurgery as the surgery of tumors of the central nervous system. They not only permitted but encouraged the general surgeon to care for the traumatic aspects of this specialty, and found partial justification for this attitude in the large numbers of such cases and the small numbers of neurosurgeons.

Today everything has changed for the better in the profession. By and large, there is a healthy understanding and co-operation between the general surgeon and the specialist. The system of closed staff hospitals, backed as it is by the American Medical Association, the American College of Surgeons, the American Hospital Association and national nurses' organizations effectively controls the caliber of the surgery done in the community served. Those who practice surgery are expected by the public to attempt only such surgery as their knowledge and ability permit. Opportunity for adequate postgraduate training is provided for all who can profit by it. Educational programs are constantly provided and the limitations of the general and special surgical procedures are taught to all who will learn. Thus the general surgeon has policed himself.

What of the specialist? He, too, has set up a method for policing himself in his own activities. Boards of certification have been created, methods of examination worked out, and lists of accredited specialists made available to the public. These are all excellent and indispensable steps in improving the care of the public by the profession. Their importance cannot be overemphasized. There are, however, still lacking certain more fundamental steps, that must be taken before the full benefit of the tremendous amount of medical knowledge at present available to the profession can reach the patient. These have to do with the teaching of the medical student. Because no one human brain can possibly hold all this information and because the student of today is the doctor of tomorrow, the student ought above all else

to leave medical school with a clear idea of his own intellectual lack and of where he can supplement it. He and the profession must learn that, from the point of view of actual use, the term "general surgeon" implies ignorance of the specialties, just as the term "specialist" implies ignorance of certain data that are made use of every day by the general man. Neither is capable of doing all things and simultaneously doing any one of them well. A general specialist is a paradox, and a dangerous one at that. So, too, is the specialist who cannot see beyond the walls of his own office. Any necessary specialization of general surgery must be duplicated by the necessary universality of the specialties. Failure to teach this in the schools and inability on the part of the profession to recognize its practical application to everyday practice are holding back the development of both specialist and general man.

As I have said, many general surgeons and practitioners and a disgracefully large number of neurosurgeons still believe that the real mission of the neurosurgeon is to deal with tumors and pain affecting the central nervous system. They will concede that the nervous system is heir to many other surgical ills, but these are regarded, on the one hand, as being too broad in scope for the specialist to deal with, and on the other, as being something to occupy an idle moment with when the neurosurgeon has no tumors or physiologic mysteries to cope with. It is not surprising that this attitude should persist. In my opinion, the educational policies of our medical schools foster it. Because of the tremendous increase in the amount of information that must be taught in four years, there is not time to teach many of the specialties adequately. Such a specialty as neurosurgery, therefore, is taught by the professor of general surgery, or else a few hours of lectures where days should be available are grudgingly granted the neurosurgeon for what use he can make of them. No attention is paid and very likely no knowledge is had of the ramifications of this specialty into almost all the other fields of surgery.

For example, the tremendous number and unjustifiably high mortality of craniocerebral injuries have been matters of common knowledge for years. As recently as the middle of October, 1942, the Mocks stated in the *Journal of the American Medical Association*:

Facts collected from various sources warrant a conservative estimate of 600,000 serious head injuries . . . as the annual incidence of this type of trauma. With average mortality rates of 10 per cent for serious head injuries without skull fractures and an average death rate of 30 per cent for proved skull fractures, it be-

comes apparent that 100,000 of our friends, neighbors and relatives are being killed — nearly 300 people each day — by brain injuries.

It is obviously impossible for the neurosurgical specialist to care for all these injured. The majority must be cared for by the general surgeon according to instruction supplied by the specialist, yet no practical effort is made to render these data available to the student, and almost none to furnish them to the house officer, who appears later among the public as a so-called "well-trained" general surgeon. Also let not the neurosurgeon who advocates, as an important part of his special training, giving two years to the study of the cellular pathology of cerebral tumors forget that it took Harvey Cushing thirty-one years to collect 2000 cases of brain tumor. Three hundred times that many brain injuries occur in the United States in one year of peace alone, and fifty times that many patients with brain injuries die as the result of them in the same period. From the viewpoint of the public, of what avail is it to teach a medical student how to deal with a cyst of the pancreas, an adrenal tumor or an internal concealed hernia, or a neurosurgical resident how to differentiate an astrocytoma and an astroblastoma, if neither is taught any of the special methods that will permit him later to reduce this tremendous number of deaths? Can a more striking example of the need for co-operation between general surgeon and specialist be instanced? Is this not the very essence of the universality of a specialty? So too, what of the specialist who receives his neurosurgical training in the leisurely field of tumor surgery, only to find that in practice he must make up his mind at once, sacrifice technical meticulousness for lifesaving speed, and learn through bitter experience that life is indeed short and decision certainly difficult? It must be apparent that in this most important field of medical education and public relations the specialty of neurosurgery has a considerable universality.

Let me give you further less striking but quite as important examples. To continue with injuries: Spinal cord injuries — not so frequent as craniocerebral injuries but more disabling — have resisted successful treatment by general surgeons and neurosurgeons for years. Patients lived in the misery of a constantly wet bed, bedsores, bouts of pyelitis and adduction and flexion contractions of the legs, only to die eventually from sepsis. By invading the field of another specialty — that of genitourinary surgery — and enlisting the help of the physiologist, a method of tidal drainage of the bladder was devised whereby these patients could

be kept dry. Coincidentally, bedsores either did not develop or healed promptly when they did. contusions could be successfully dealt with by operation or splinting under the direction of the orthopedic surgeon. pyelitis disappeared, and major genitourinary sepsis was reduced from 72 to 16 per cent. with a corresponding lowering of the mortality.

Pain in the face is a common symptom. If it comes as lancinating attacks limited to one side of the face and can be constantly reproduced by stimulation of one so-called "trigger zone," the patient is suffering from *tic douloureux* or trigeminal neuralgia. This is strictly a neurosurgical problem. It can be dealt with only by appropriate denervation. Nevertheless, all neurosurgeons will testify that most sufferers from this terrible disease have had many or all their teeth pulled out, at least one antrum of Highmore opened, and other nasal operations galore performed by a dentist or rhinologist before getting to the neurosurgeon. Here the dentist and rhinologist must recognize their own deficiencies and make use of the specialist. On the other hand, the neurosurgeon must not forget his own restricted knowledge when trying to deal with patients who have equally severe but less typical facial pain. Pulp stones, malocclusion, and apical infections all are frequent causes of this pain, and all are familiar to the dentist and completely unfamiliar to the neurosurgeon. So, too, affections of the sphenopalatine ganglion, hypertrophied turbinates, a deviated nasal septum, shingles and degenerative changes of the basal ganglia associated with cerebral arteriosclerosis can and often do cause facial pain that mimics closely the classic symptoms of trigeminal neuralgia. Denervation of the face in such cases gives no relief of symptoms. Although the former are old stories to the rhinologist and the latter the same to the general medical man, the neurosurgeon must admit ignorance of their characteristics, diagnosis and treatment except in their most superficial aspects.

Ménière's syndrome or disease, to use the familiar term, is first seen by the otologist. At that time the differential diagnosis includes a number of possibilities. Among the common causes of the syndrome may be an eardrum that needs splinting, a blocked eustachian tube, infectious or other forms of acute labyrinthitis and a tumor of the cerebellopontine angle. What more perfect example of the need for co-operative diagnosis and therapy between specialists could be cited, increased as it may be by the possible need for the services of the allergist, the biochemist and the ophthalmologist? Yet such co-operation

cannot even be begun until each doctor concerned recognizes his own intellectual and technical limitations and turns for help to the others when he has reached these limits. The universality of such specialization pays high dividends in grateful and relieved patients, whereas an attempt to generalize a specialty or specialize a general problem leads to nothing but grief for all concerned.

Appropriate cases could be multiplied many times. Headaches, the bane of every professional man's existence, tax the powers of every branch of medicine and surgery, from the gynecologist and endocrinologist to the neurosurgeon and psychiatrist. Low-back pain and the problem of ruptured intervertebral disks have taught the orthopedist that "radiculitis" is more than a fancy word, and the neurosurgeon that some knowledge of bodily mechanics is essential to the proper examination of a back. Brain abscesses and their relation to ear disease make a team of the otologist and the neurosurgeon. The dermatologist who must deal with the distressing symptoms of hyperhidrosis, the obstetrician and pediatrician with their problem of craniocerebral injury to the newborn and the electrophysicist with his unsung contribution to the study of epilepsy are other examples of the need for co-operation between doctors.

Industry has an interest in this. It is probably correct to say that the late effects of injuries to the head and back constitute one of the most difficult problems of industry, and one that is yet unsolved. A study of the records of any impartial examiner—for the Massachusetts Industrial Accident Board, for example—indicates that the chief reason for this is that the claimant, the insurance company and industry itself have for years demanded a definite diagnosis at a minimal cost at the earliest possible moment after the receipt of the injury. The effect of this has been to limit early hospitalization and adequate consultation. It has forced the doctor to make a diagnosis without adequate facts or study. This in turn has led the claimant to become suspicious of the profession and unco-operative with those who may actually have his best interests at heart. The patient turns toward the untrained overworked surgeon, medical man or general practitioner, who has neither the time nor the financial or intellectual assets to have investigations carried out along specialist lines, but who continues to be employed because he is known to be sympathetic with the patient. He sticks to his diagnosis right or wrong, and is often forced to perform underpaid work badly for lack of anything better to do. The crying need in the solution of these difficulties is not to take the patient away from his

doctor, but rather to make it easy for both to have the courage to recognize that the case calls for the use of other professional brains. Only in this way will claimants, insurers and insured get the most benefit from the universality that is inherent in all specialties and particularly in neurosurgery.

I have offered nothing but destructive criticism. That the specialties in general and neurosurgery in particular have a universality cannot be denied, but this is, I fear, not well recognized. What can be done to correct this lack? No move in that direction will be successful until the doctor is taught while still a medical student not to say, "How much I know!" but rather, "How much I *don't* know!" With that concept firmly implanted in his mind and in the minds of his teachers, he and they will see to it that he has a broad general training during his medical-school and hospital years. Part of that training will consist in impressing him with the need and value of tapping other peoples' brains, and with the realization that if he would increase his special knowledge, that increase can come only at the expense of his general information. Specialists must not even be formed in embryo in the medical school. I do not mean that students should not be taught by specialists, but that this teaching must be from the point of view of the general applicability of the specialty. Most important of all, when a specialty is taught by a general surgeon or physician, this must be done from the

point of view of the special applicability of the general problem.

Such teaching can have no effect for some years, however fundamental, necessary and overdue it may be. What can we do today? First and foremost we should concentrate our postgraduate education not on teaching new facts to the profession, but rather on impressing them with how many of the old facts they do not know or have forgotten. They will soon find how much happier they are when they learn to say to a patient, "I don't know but will find out," rather than "I don't know, but no one else does either, so it's no use consulting other physicians." As another part of an all-over effort to instrument this universality of the specialties, certifying boards should emphasize the important general aspects of the specialty, minimize the highly technical and special knowledge that is at present rather overvalued, and see to it that the candidate knows what he does not know and understands how to get that knowledge from others who do. Finally, let the specialist himself beware of becoming so superspecialized that he loses touch with reality and becomes a drag on the wheels of progress, instead of acting as a spur to the general surgeon, medical man and practitioner in their attempts to improve their care of the public. Only in this way will the foundations of the practice and the art of medicine be built up into a structure that is free from weaknesses and strong enough to last forever.

SINGLE TRUE CYSTS OF THE SPLEEN*

Reports of Three Cases

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BOSTON

THE rarity of splenic cysts is attested by the fact that up to February, 1941, McClure and Altemeier¹ were able to find only 148 cases of all types reported in the literature. Denneen² mentions that at Bellevue Hospital from 1904 to 1940 only 8 cases were revealed in the records of the Pathology Department.

The occurrence of various types of cysts in the spleen has led to the proposal of several classifications of these tumors that seem to be unnecessarily complicated and unimportant. Of these, that recently proposed by McClure and Altemeier¹ appears to be the best. All cysts of the spleen may be grouped under two headings, the true and the false, depending on whether or not they are lined by a specific secreting membrane.

True cysts are much less frequent in occurrence than are the false cysts. Of the 137 cases collected from the literature by Fowler,³ 21 per cent were of this variety. The 3 cases reported here were large unilocular true cysts, each with a specific lining membrane.

DIAGNOSIS

Because cysts of the spleen are encountered so rarely, the impression exists that the diagnosis is difficult. This is no doubt the case when they are small. Large cysts, however, present a clinical picture which is so characteristic that the diagnosis can be readily made. The subjective symptoms, excepting for the fact that a tumor is noticed, are so negligible that the clinical history is of little value. A dull dragging pain or discomfort in the left upper quadrant of the abdomen may be complained of. From the diagnostic standpoint the greatest help is to be obtained from the physical examination and the roentgenological findings. The significant data in the 3 cases subsequently reported are listed in Table 1.

Physical Examination

There is always a large abdominal tumor that on careful palpation is found to occupy the left upper quadrant of the abdomen, whence it extends into the lower abdomen and toward the right side to an extent depending on its size. The left costal margin is usually pushed outward by

the tumor, which always extends beneath it. This does not as a rule occur in pancreatic cysts, and rarely occurs in ovarian ones. The lower border of the tumor even when very large does not occupy the pelvis in the way an ovarian cyst does. That the tumor is cystic can often be determined by the sensation of resiliency imparted on bimanual palpation. A definite fluid wave can usually be detected in large cysts. This was so in the largest two of the three tumors in this series.

X-Ray Examination

When all the evidence is assembled, the roentgenologic examination in cases of large splenic cyst is so typical that it may for all practical purposes be considered diagnostic. The left side of the diaphragm is high, and under the fluoroscope its motion is impaired. A plain abdominal plate shows a large, soft-tissue mass arising in the left upper quadrant. Hampton⁴ has called attention to the fact that the lower pole of this shadow in cases of splenic cyst has a somewhat angular, almost pointed contour that extends downward and to the right into the pelvis. This observation is based on the appearance of the shadow cast by the tumor in the 3 cases reported here, and depends on the fact that in all these cases the cyst developed in the upper pole of the spleen, leaving a small, intact, triangular lower pole at the lower extremity of the tumor. If the cyst should happen to develop in the lower pole, this finding would doubtless not occur. After a barium meal the stomach is found to be pushed to the right, and if the tumor is a large one it is pushed backward as well. The colon, especially the transverse, splenic flexure and descending portions, is found displaced downward and to the right. The left kidney as visualized by intravenous pyelography is shown to be pushed downward by the tumor. The contour of the kidney pelvis is usually not altered.

In any case of large abdominal tumor that appears to arise from the left upper quadrant of the abdomen and feels cystic on palpation, the above-described x-ray findings are practically diagnostic of cyst of the spleen. Some of these are well demonstrated in the roentgen-ray films of Case 1, which are reproduced in Figures 1, 2 and 3.

*Prepared for presentation at the canceled 1942 meeting of the New England Surgical Society.
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TREATMENT

In the present state of surgical knowledge and experience, it is useless to describe the obsolete operations of marsupialization, incision and drainage, or local excision or enucleation of these cysts. Splenectomy is by far the simplest and

TABLE 1. Significant Data in 3 Cases of Large, Single True Cyst of the Spleen.

DATA	CASE 1	CASE 2	CASE 3
Age	19 yr	23 yr	8 yr
Sex	F	F	M
Symptoms			
Duration of abdominal swelling	2 yr	9 yr	10 wk
Dull pain (in left upper quadrant)	+	0	0
History of trauma	0	0	0
Physical examination			
Tumor apparently arising in left upper quadrant	+	+	+
Left costal margin pushed outward	+	+	—
Tumor cystic feeling	+	+	+
Fluid wave detected	+	+	0
X ray examination			
High left diaphragm	+	+	+
Limitation of motion of diaphragm	+	+	+
Mass in left upper quadrant	+	+	+
Small triangular lower pole at lower extremity of mass	+	+	+
Stomach displaced to right	+	+	—
Stomach displaced to right and posteriorly	+	—	—
Stomach displaced to right and downward	—	+	—
Colon displaced downward and to right	+	+	—
Left kidney displaced downward	+	+	+
Restoration of stomach colon and left kidney to normal after splenectomy	+	—	—
Pathological examination			
Size of tumor	45 by 30 by 30 cm.	30 by 30 by 17 cm.	11 by 16 by 17 cm.
Weight of tumor	17 3 kg.	4 7 kg.	?
Nature of fluid contents	Thin, dark-red and hemorrhagic	Thick and brown (3 liters)	Thin, turbid and brown
Nature of cyst			
Type	Unilocular	Unilocular	Unilocular
Walls trabeculated	0	+	+
Lining membrane	+	+	+
Nature of lining membrane	Thin layer of flattened endothelial-like cells	Thin layer of flattened endothelial cells	Single layer of cuboidal cells
Splenectomy performed	+	+	+
Result	Cured	Cured	Cured

safest procedure and should be adopted in all cases.

All recent reports agree that splenectomy in these cases is a safe and reasonable procedure, with a mortality of not more than 4 per cent.³ There is a rapid restoration of the normal rela-

tions of the viscera that were displaced by the tumor. The roentgen-ray proof of this is well borne out in Case 1. A plate from this case (Fig. 5) shows that before the patient left the hospital the stomach and colon were back in approximately normal position.

CASE REPORTS

CASE 1. L. S., a 19-year-old girl, was admitted to the Massachusetts General Hospital on March 22, 1940, complaining of a gradually enlarging abdomen. Approximately 2½ years before admission she first noted the presence of a steady, dull, somewhat ill-defined aching pain in the left upper quadrant of the abdomen beneath



FIGURE 1. Case 1.

The plain abdominal film shows a large splenic cyst

the rib margins. This discomfort continued, and 2 years before entry she noticed a lump in the left upper abdomen in the same vicinity in which the pain was arising. She was otherwise well and led a fairly normal life until 6 months before admission, when she became cognizant that the same quadrant of the abdomen was swelling. It seemed to enlarge to the left and was definitely hard. With this enlargement the patient experienced mild distress in breathing deeply and complained of a sensation of fullness after the ingestion of moderate-sized meals. The constant pain had many superimposed sharp twinges. There was no vomiting, but for several months there had been slight morning nausea. She denied pregnancy and stated that her catamenia had been normal. The last menstrual period occurred 5 days before admission and the one previous to that occurred 3½ weeks before admission, with normal flow and no clots or pain. During her illness there had been no change in weight. She noted an increasing ease of fatigability and, because of the abdominal mass, discomfort while walking

Physical examination revealed a healthy appearing, obese girl. She had a very slight mustache, with stiff but sparse hairs on the chin, hairs on the chest and a masculine distribution of the pubic hair. Examination of the heart and lungs was negative. The blood pressure was 130/100. The abdomen was protuberant and slightly asymmetrical so that the left upper quadrant bulged slightly more than

defined. Intravenous pyelograms showed that the dye appeared promptly on the right side and that the right pelvis and calices were normal. On the left in one of the films there was a small quantity of dye visualized in a region that probably represented the pelvis of a normal left kidney. The calices were incompletely demonstrated. The left kidney was displaced downward. All the visible bones appeared definitely older than indicated by the patient's age. This was particularly true of the lower lumbar vertebrae which showed wavy configurations of their surfaces. All the visible epiphyses were closed. A chest plate revealed a high diaphragm regular in outline. The lung fields were clear. The heart was normal in size and shape. There was no evidence of metastases. By fluoroscopy the left side of the diaphragm was seen to move poorly while the right side showed fair motion. A barium meal with fluoroscopic observations showed that the stomach and small intestines were markedly displaced to the right and posteriorly by



FIGURE 2 Case 1

The film of the upper gastrointestinal tract shows that the stomach and jejunum are pushed to the right side of the abdomen by the cyst

the right. On palpation a cystic smooth, ovoid tumor mass was noted, which transmitted a good fluid wave. There was no shifting dullness in the flanks. The tumor moved slightly on respiration. Pelvic examination showed a slightly enlarged nulliparous cervix.

Examination of the blood showed a red cell count of 4,700,000, with 75 per cent hemoglobin, and a white-cell count of 12,600, with 75 per cent neutrophils, a smear was essentially normal. The stools were negative for occult blood. A blood Hinton test was negative. The serum nonprotein nitrogen and protein levels were normal. A sugar tolerance test showed the following findings: fasting 74 mg per 100 cc, 30 minutes, 176 mg, 1 hour, 167 mg, 2 hours, 77 mg. Urine examinations showed specific gravities of 1.018 to 1.028 and 0 to ++ tests for albumin, and the sediment contained 5 to 10 white cells per high power field. A urine culture showed a moderate growth of nonhemolytic streptococci. The vital capacity was 3250 cc. A 17-ketosteroid determination was normal (9 mg per 100 cc).

Röntgenograms of the abdomen revealed an unusually large soft tissue mass completely filling the upper abdomen and extending downward to the level of the lower border of the left sacroiliac joint (Fig 1). The margins of this mass were smoothly rounded and sharply

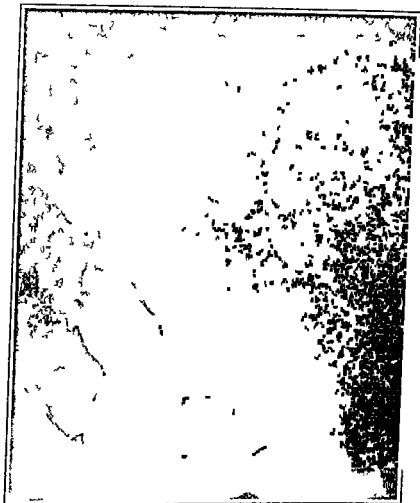


FIGURE 3 Case 1

The barium enema demonstrates that the transverse and descending portions of the colon are pushed downward by the cyst

the huge mass (Fig 2). A barium enema revealed that the splenic flexure was markedly displaced downward by the tumor mass, the transverse colon running along the lower edge of the tumor (Fig 3). The hepatic flexure was not displaced.

On April 5 the patient was operated on. A long left rectus muscle splitting incision was made extending from the umbilicus to within 5 cm of the pubes. The abdomen was opened and the tumor was found to be an immense cyst of the spleen arising from the upper pole. The lower pole was easily identified and extended into the pelvis. The vessels of the splenic pedicle entered the tumor at its lower portion. These were easily ligated

and the lower portion of the spleen was freed. There was a dense adhesion of the cyst to the left lobe of the liver, which had been thinned out over a portion of the tumor, and several other dense adhesions to the peritoneum and diaphragm. The stomach, colon and small intestines were not adherent to it. The kidney had been

ach and colon had returned approximately to their normal positions. She was discharged on the 17th postoperative day.

CASE 2. M.S., a 23-year-old woman, was admitted to the Baker Memorial on August 2, 1932, because of a large

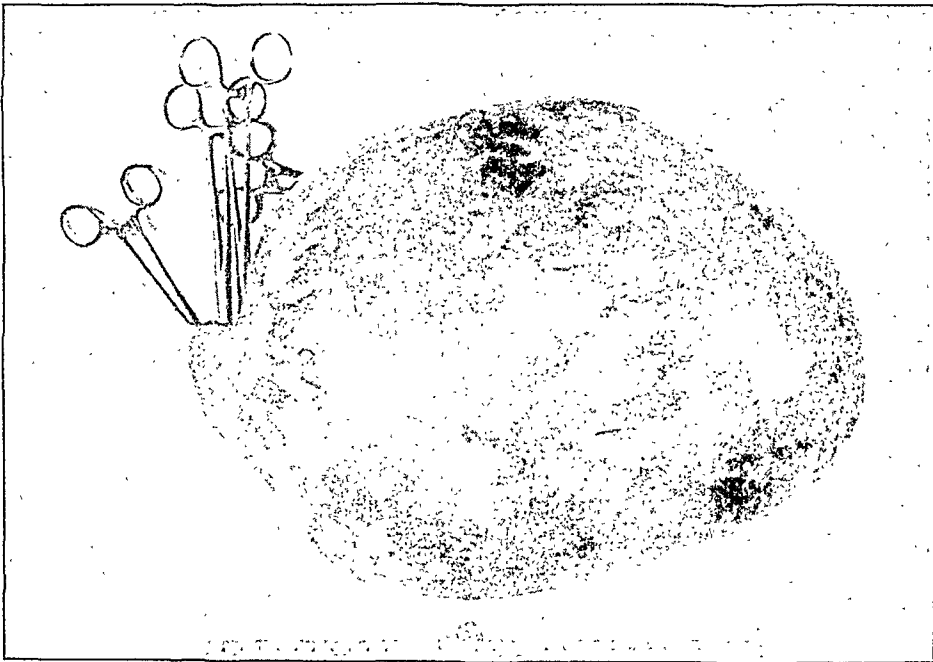


FIGURE 4. Case 1.

This is a photograph of the cyst taken soon after removal. Note the lower pole of the spleen, which gave rise to the pointed contour at the lower extremity of the x-ray shadow.

markedly displaced downward by the tumor, the upper end of which occupied the right upper half of the abdomen from front to back. It seemed to contain many areas of necrosis or at least of hemorrhage into its substance. After removal of the tumor without breaking it, many small bleeding points in the undersurface of the diaphragm were tied off and the abdominal wound closed in layers in the usual way.

Pathological examination showed a tremendous, tense, partly red-brown and partly grayish, smooth-walled, ovoid cyst measuring 45 by 30 by 30 cm. and weighing 17.3 kilograms (38 pounds), the upper portion of which was intimately blended with and appeared to arise from the spleen, measuring 8 by 5 by 5 cm., which was splayed out over the cyst (Fig. 4). There were a few fibrous shreds scattered over the surface of the cyst and also a few small, whitish areas. On palpation a fluid wave was present. The cyst was found to consist of a single large cavity filled with dark-red hemorrhagic fluid and having a tough and apparently fibrous wall. It was lined by a thin, flattened, endothelial-like membrane and was completely encapsulated by relatively dense connective tissue. No definite indication of the origin of the lesion was apparent. A diagnosis of splenic cyst, unclassified, was made.

The patient stood the operation well and her convalescence, though briefly complicated by collapse of the left lower lobe, was rapid and essentially uneventful. A postoperative x-ray film (Fig. 5) showed that the stom-

ach and colon had returned approximately to their normal positions. She was discharged on the 17th postoperative day.

abdominal mass. Nine years previously when she was undergoing a routine physical examination a large, firm, solid mass had been found in the left upper quadrant of the abdomen. She was told at this time that the mass was a large spleen and would cause her no trouble. She was thoroughly studied by x-ray and blood studies were done, and a diagnosis of splenomegaly was made. The mass continued to enlarge and doubled its size in 6 years, but there was still no discomfort from it. It filled the entire abdomen, but was larger on the left than on the right. Although the patient had been barred from all athletics during her college course, she had not considered herself handicapped by the tumor. She had never been jaundiced. There had been no evidence of any ovarian disorder; her periods had been as regular as usual, with no metrorrhagia and no menorrhagia. She had bled rather freely after a tonsillectomy 6 years previously and at another time after a tooth extraction. The appetite was good. The bowels moved freely once a day without catharsis and the patient had passed no bloody or tarry stools. She had no urinary symptoms.

Physical examination revealed a well-developed and well-nourished young woman in no distress. The heart was normal. The blood pressure was 118/76. In the left upper quadrant of the abdomen there was a deformity of the rib margins due to pressure from within. A nontender, firm cystic mass could be felt in this region. There was definite elasticity and fluctuation. There were

no other masses in the abdomen. The cyst extended well out into the flank.

X-ray examination showed a huge, soft tissue tumor occupying the upper two thirds of the left side of the abdomen. It displaced upward the left side of the di-

aphragm and the whole tumor was turned out of the abdominal cavity. There was comparatively little bleeding. All divided arcs were covered with peritoneum and the wound was closed without drainage. The appendix was removed and the stump buried.

Pathological examination showed a tumor measuring 30 by 30 by 17 cm. and weighing 47 kilograms (104 pounds) covered by splenic tissue only a 12-by-4-by-2-cm. piece of actual spleen remaining. A large white area 14 cm. in diameter was seen on one surface. The remainder of the surface was deep red. The tumor was fluctuant. It was filled with 3 liters of thick brown fluid. The walls were tabulated whitish and entirely fibrous. The appendix was slightly thickened with a fecalith 3 mm. in length in the distal portion of the lumen. A diagnosis of cyst of the spleen and healed appendicitis was made. The wall of the cyst was made up of dense bands of fibrous tissue. An inner lining could not be



FIGURE 5 Case 1

The postoperative film of the gastrointestinal tract shows that the stomach and jejunum have been restored to normal position.

aphragm which was limited in excursion but smooth in outline.

Fluoroscopic examination of the chest showed no other variations from normal. What appeared to be the kidney outlines were unusually low in position. The edge of the liver also appeared low. Small collections of gas were seen in the bowel and these gas bubbles were markedly displaced downward and to the right. What probably represented a gas-filled stomach lay in the right lower quadrant. The lower edge of the tumor was sharp in outline and descended below the crest of the diaphragm (Fig. 6). The right edge was 4 cm. lateral to the vertebrae and within the right edge of the tumor one small area of calcification was seen. There was no evidence of erosion of the vertebrae or ribs. There was some kyphosis at the dorsolumbar junction and upward displacement of the ribs.

On August 4 the patient was operated on. A left paramedian incision was made and a large tumor was seen beneath it. This was found to be a large cyst of the spleen that had thinned out the whole spleen except for an area 5 cm. in width and 8 cm. in length at the lower pole. The rest of the spleen was spread out over the anterior and posterior surfaces of the tumor. The tumor was adherent posteriorly and especially to the diaphragm. The pedicle entered the lower pole of the spleen. This was tied off the adhesions were separated

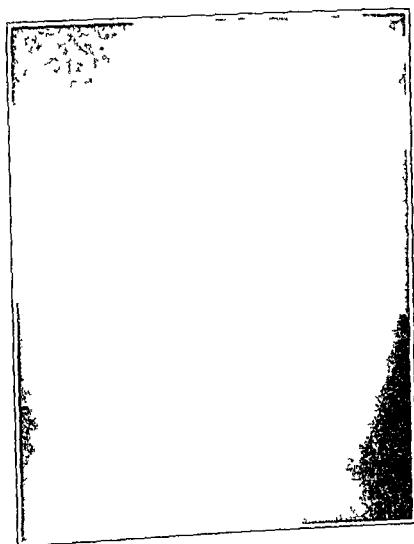


FIGURE 6 Case 2

The plain abdominal film clearly illustrates the pointed contour at the lower extremity of the shadow.

made out possibly because of long fixation before opening. A thin layer of flattened endothelial cells was vaguely outlined.

Following operation the patient made an uneventful recovery and was discharged on the 15th postoperative day.

CASE 3 R. U., an 8-year-old boy was admitted to the Baker Memorial on February 2, 1931 because of swelling of the left side. Ten weeks previously a swelling had been noted on the left side below the rib margin. From then until admission it seemed to be getting gradually larger, although it had been painless and there had been no associated symptoms other than some loss of weight.

The patient's appetite had always been poor and he was extremely constipated, requiring a laxative about once a week. There were no genitourinary symptoms.

Physical examination was negative except for a large, rounded elastic tumor palpable in the left upper quadrant.

X-ray examination of the chest revealed the diaphragm high on the left side and slightly limited in excursion. It was normal in outline and moved well on the right. Examination of the genitourinary tract showed massive soft-tissue dullness in the left upper quadrant, apparently displacing the left kidney downward and extending to the level of the fourth lumbar vertebra. The mass was roughly triangular and in the anterior-lateral position. The upper pole of the left kidney was at the level of the second lumbar vertebra and the lower pole opposite the fourth lumbar vertebra, but other than this the left kidney was not abnormal. X-ray examination after the injection of Uroselectan failed to give any additional information.

On February 5 an operation was performed. A vertical incision was made extending from the ensiform nearly to the pubes. There was a large cyst of the spleen. The vessels on the inner side of the tumor were clamped and cut, and the adhesions of the diaphragm and under-surface of the tumor freed by blunt dissection or cutting. After the tumor had been freed it was found to be so large that it was almost impossible to deliver it, as it seemed to be wedged tightly between the chest wall and the vertebral column. This was accomplished, however, with little bleeding. The denuded areas were covered with peritoneum except those on the diaphragm where the adhesions had been cut, and the wound was closed without drainage. The liver was normal in size and color. There were no enlarged lymph nodes and there was nothing suggesting malignant disease.

Pathological examination showed a purplish-red cystic tumor measuring 11 by 16 by 17 cm., with a smooth

surface and resembling the spleen. The spleen itself was compressed and formed a large portion of the wall of the cyst. At the poles of the cystic mass the splenic tissue was more abundant. For about half its circumference where it was uncovered by the spleen the wall was thin and fibrous. The cyst was filled with thin, turbid, brown fluid. The inner surface was smooth and in places showed coarse trabeculations. On microscopic examination it was found to be lined by a single layer of cuboidal cells. The adjacent walls were composed of degenerate fibrous tissue. The sinuses of the spleen were dilated, the lymph follicles were diminished, and the reticulum was prominent. The gross and microscopic appearances were suggestive of an origin from a lymph sinus. A diagnosis of simple cyst was made.

The postoperative course was uneventful and the patient was discharged on the 16th postoperative day.

SUMMARY AND CONCLUSIONS

The findings of physical examination of the abdomen taken with the characteristic x-ray appearances should enable one to make a diagnosis in cases of large true cyst of the spleen.

Following splenectomy the abnormally displaced stomach, colon and left kidney assume their normal positions.

Three additional cases of large single true cyst of the spleen are reported.

205 Beacon Street

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ROENTGENOGRAPHIC SURVEYS FOR TUBERCULOSIS IN MASSACHUSETTS AND THEIR IMPORTANCE TO THE PHYSICIAN

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THE war has brought some danger of a rise in the prevalence of tuberculosis but it has also brought a tuberculosis case-finding project of far greater magnitude than any previously contemplated. The United States Army, aided at the beginning by the Massachusetts Department of Public Health, is engaged in making 4-by-5-inch stereoscopic photofluorograms of the chests of all men inducted under the Selective Service Act or volunteering for enlistment. These films are interpreted before the completion of the physical examination. In addition, the United States Navy is making routine 35-mm. photofluorograms of enlisted men at naval training stations. More than 2000 men have been rejected for military service in Massachusetts by the Army alone because of tuberculosis or suspected tuberculosis.

The names and addresses of Army rejectees are forwarded from the examining station to the Department of Public Health. The state district health officer, working through the local board of health, later attempts to secure answers to the following questions on each case:

Has the patient been x-rayed again? If so, by whom?

State the findings.

Was the diagnosis of tuberculosis confirmed? If so, has the case been reported?

What further study or treatment has been recommended? Is this being carried out?

If the diagnosis was confirmed, give the number of household contacts, the number who have been x-rayed and the names of any found to have tuberculosis.

In the field of industry routine chest x-ray films are also coming into frequent use. Several large plants in Massachusetts employing thousands of men have recently made them a part of every pre-employment examination, and the opportunity of a survey of all workers will soon be offered to many other plants if present plans are carried through. Many colleges likewise require x-ray examination of students. Cases discovered through industrial surveys conducted by the Department of Public Health are handled as follows: the individual is told that he or she has a chest condition needing treatment or further study and is asked to designate a physician to whom the roentgeno-

graphic report can be sent. Only if the patient states that he has no physician, cannot afford one or has no intention of going to one is the alternative of attendance at a tuberculosis clinic suggested.

Physicians may, therefore, expect to see numbers of men and women who have been told that they have tuberculosis and referred to their own doctors for advice, treatment or further study. Cases thus referred can be classified in several groups. The simplest is the obvious case of *active tuberculosis* needing sanatorium treatment and, possibly, collapse therapy. Repetition of the x-ray examination is often unnecessary, especially if partial confirmation is obtainable by physical examination. There are three steps to be taken: reporting the case, arranging for admission to a sanatorium and examining by x-ray all household contacts. It is sometimes assumed that because a state clinic has made the x-ray examination these cases are already reported, but this is not correct; reporting is left to the physician. Diagnosing and reporting tuberculosis on the basis of x-ray evidence alone sometimes results in errors.

A second group has been classified on the basis of x-ray findings as *tuberculosis suspects*. This generally means that the roentgenologist has seen a small hazy or infiltrative shadow but is not sure enough of its presence or significance to label it pulmonary tuberculosis. These patients invariably should have another film taken. If the technic is better, sometimes this alone decides the question; or the lesion previously seen may have disappeared, indicating that it was an acute pneumonitis. More often, however, the second film, particularly if taken after a short interval, merely provides a basis for comparison with subsequent ones, since the original survey film is not usually available for this purpose. Symptoms and physical signs are unlikely to aid in the diagnosis, since they are not usually elicited in such early cases. Changes in the differential leukocyte count, an afternoon fever and an elevated sedimentation rate may have confirmatory value, but one should not wait for their appearance to institute treatment; furthermore, they are not specific for tuberculosis. Once in a while tubercle bacilli are found in the sputum or gastric contents of a suspect by culture or guinea-pig inoculation, but this occurs

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seldom to be of great assistance. Serial roentgenograms are the only reliable test. Their frequency depends on the patient's age, the nature of the lesion and the opinion of the roentgenologist. In young adults, they may be spaced from one to four months apart at first. Persistence of the lesion unchanged may indicate stability or may be a sufficient reason to institute treatment, depending on the radiologic appearance. Evidence of gradual regression or fibrosis is proof of recent activity and hence may call for even more frequent observation than a stable lesion.

Many of these remarks apply with equal force to the third group, called *inactive or healed tuberculosis*. It is advisable to obtain a roentgenographic record of the cases classified as healed, and if there is any doubt about their status, especially if the patients are young and the lesions are of more than minimal extent, they should be kept under periodic x-ray observation until the physician is satisfied that they are inactive. Occasional misunderstandings arise through the confusion of the stage of disease with the question of activity. A classification of minimal, moderately advanced or advanced refers solely to the extent of involvement, not to the activity of disease; "minimal active tuberculosis" and "far-advanced inactive tuberculosis" are correct expressions. The standard basis for classification both of extent of disease and of clinical status is that of the National Tuberculosis Association. Patients are divided according to clinical status into five groups—apparently cured, arrested, apparently arrested, inactive and active. No such exact classification can be made or is attempted from a single observation. There is even a large error in classifying cases simply as active or inactive on the basis of one x-ray film without the assistance of clinical study, although if cavities are visualized there is no question.

Primary phase tuberculosis is a diagnosis frequently made but seldom of any clinical significance in adults. It is rarely seen in an active stage; usually it is manifested by one or more calcified parenchymal nodes or tracheobronchial nodes or both, constituting a calcified primary complex. The Army rejects these men if the lesions exceed certain limits of size or number. The Department of Public Health does not refer to such cases at all when they are encountered in industrial surveys, unless the appearance of the lesion is most unusual. Inactive primary tuberculosis is not reportable and does not require treatment. If the parenchymal calcifications are multiple and associated with some fibrosis, it may be impossible to distinguish them from healed reinfection-type pulmonary tuberculosis unless the whole course of their development has been watched. Active primary tuberculosis, of course, is reportable and re-

quires attention. It often cannot be differentiated from reinfection-type tuberculosis.

Pleurisy with effusion is rarely found in these surveys. Evidence of old pleurisy, such as obliterated costophrenic angles, is of common occurrence, but requires no attention unless the attack occurred within the past five years.

A great many *nontuberculous lesions* are found, some of which are unavoidably mistaken for tuberculosis. Acute respiratory infections, including the so-called "virus pneumonias," may be encountered in ambulant persons who think they have an ordinary cold. If the true nature of these is suspected, re-examination in four to six weeks is advised; the shadow will then have disappeared. Bronchiectasis, atelectasis, suppurative lung abscess, lymphoma, sarcoid, cystic disease of the lung and primary or metastatic carcinoma of the lung are occasionally seen. Emphysema and generalized pulmonary fibrosis, idiopathic or secondary to some other condition, may be recognized. Spontaneous pneumothorax is rarely discovered.

Cardiac lesions are often found in persons who did not know of their existence, sometimes even with signs of pulmonary congestion. Rheumatic, hypertensive, syphilitic and occasionally congenital types of heart disease may be encountered. Diaphragmatic hernias, situs inversus and spine or rib anomalies are seen.

* * *

Physicians in all parts of the State have diagnostic x-ray service available for patients who cannot afford to go to a roentgenologist. All the public sanatoriums maintain outpatient departments, most of them have consultation clinics, and the large cities have their own dispensaries with x-ray facilities. Reports are made to the referring physicians. Sputum examinations are performed without charge by the Bacteriological Laboratory at the State House and by the health-department laboratories in Boston and other large cities. The search for acid-fast bacilli in a stained smear, incidentally, is coming to be regarded as a rather crude test; many cases are positive only on a concentration test, guinea-pig inoculation or culture. The last-named modification as now carried out is an inexpensive, highly sensitive procedure that is being used more widely than before. It reveals the organism in so many patients who were not formerly suspected of having active disease that ideas regarding the significance and frequency of positive sputums have had to be somewhat modified. When smears are negative in a case with clinical evidence of activity, the more sensitive methods of examination should be tried. Patients who do not expectorate may show tubercle bacilli of gastric lavage.

It should be remembered that tuberculosis is a disease of adults and is seldom found in children after infancy and before adolescence; that its prevalence tends to increase with age from adolescence on; that the frequency of inactive disease also increases with age; that the majority of reinfection-type lesions found in young persons are unstable; and that many lesions in older persons are a greater source of danger to their associates than to themselves. These epidemiologic points are given detailed consideration by Chadwick and Pope¹ in their monograph on the public-health aspects of tuberculosis.

A tuberculosis specialist in Boston has repeatedly stated that physicians are not interested in tuberculosis because the State has so largely taken over its treatment. There is truth in this assertion, as shown by the fact that the Section on Tuberculosis of the Massachusetts Medical Society was discontinued for lack of attendance at the annual meeting. Three factors in tuberculosis—its well-known association with poverty, its chronicity and its contagiousness—have been responsible for its control having been largely assumed by public and voluntary agencies. The majority of patients can neither support their families nor pay for treatment during the necessarily long periods of hospitalization. Public ownership and operation of sanatoriums and clinics were inevitable and need no defense at this late date, for they have unquestionably been the most effective means of making adequate treatment available to every patient. However, this has taken away from the majority of physicians the opportunity of seeing the various features and manifestations of tuberculosis. Yet, private practitioners must make the initial diagnosis in most cases. It is highly important that this diagnosis be made as early as possible, for two obvious reasons: to institute treatment before it is too late, and to prevent the spread of the disease to others. In this respect the program has failed. Sanatorium records show that the proportion of far-advanced cases admitted for the first time has not declined and that the proportion of minimal cases has not risen, in spite of the wider use of x-ray films. X-ray study is finding early cases, but the numbers thus found are still too small to influence greatly the stage of disease on admission. Surveys cannot reach everyone; the public must be educated to consult a physician earlier, and the physician must be on the alert.

There is still aversion on the part of some doctors to reporting cases to the local board of health, because they think it will do no good, will result in unwarranted interference with the patient's private affairs or will prove embarrassing to him.

Others neglect to report cases because of indifference or pressure of work. Many cases come to the attention of health departments only at the time of death.

If the value of reporting can be convincingly shown, physicians will not fail to report their cases at the time of diagnosis as required by law. The responsibilities that the local board of health assumes, or should assume, when a case is reported include the following: making arrangements for admission to a sanatorium, if necessary; instructing the family in the precautions to be observed while the patient is at home; seeing to it that all household contacts are x-rayed and that those requiring further periodic examinations receive them; helping the family to obtain public assistance, when needed; and keeping in touch with the patient after his return from the sanatorium, in order to assist with any new problems that may arise.

Few physicians have the time or inclination to bother with these details, yet they are important. The board-of-health nurse should be given freedom to work with the families of tuberculous patients, and this assistance is almost always welcomed when the family understands its purpose and has become acquainted with the nurse. If, however, at the time of report the physician indicates that he wishes to assume all the responsibilities mentioned above, the local board is willing to have him do so. It was the opinion of the late Dr. Frederick T. Lord,² who served as president of the Massachusetts Tuberculosis League during the last few years of his life, that more aggressive measures should be taken by boards of health to enforce the laws and regulations for case reporting, case supervision and examination of contacts.

* * *

There is great satisfaction to the physician, and great benefit to the community, in having made an early diagnosis and instituted treatment in a case of tuberculosis, and having perhaps found a second case among the family contacts. It is not known just how many cases are thus prevented, but unfortunately there are numerous examples of fatal tuberculous disease in infants exposed to parents or others with open tuberculosis. Case-finding surveys will initiate the attack on unsuspected tuberculosis, but the physician must carry it through.

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MEDICAL PROGRESS

SKIN CHANGES OF NUTRITIONAL ORIGIN (Concluded)*

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PITYRIASIS RUBRA PILARIS

PITYRIASIS rubra pilaris is a chronic benign dermatosis with a varied course.⁸³ It may show a familial trend.⁸⁴ The basic lesion is an acuminate, horny papule involving the follicular orifice. The papules always remain discrete, giving the skin the feel of a nutmeg-grater.⁸³ The presence of these lesions on the dorsum of the fingers is especially characteristic. Dryness of the skin, with a tendency to fissuring and, when severe, to desquamation, are present. The palms, soles, elbows and knees are horny and thickened and yellowish. The face looks waxy. The skin thickens and is inelastic. Most cases are seen in young adults, but the condition may occur at almost any age. There are no constitutional symptoms and the general health is unimpaired.⁸³⁻⁸⁵ "The essential pathologic process of pityriasis rubra pilaris is follicular hyperkeratosis."⁸³

The resemblance of this dermatologic disorder to the skin lesions of avitaminosis A was early commented on by Pettler,⁸⁶ and Sutton and Sutton.⁸⁵ The last-named authors state, "The similarity of the lesions [of pityriasis rubra pilaris] with those of avitaminosis A is noteworthy, and we add here that these conditions are indistinguishable as judged by the literature, photographs and photomicrographs."

The important work of Brunsting and Sheard¹⁸³ has done much to clarify the basic understanding of this disorder and to stimulate a renewed interest in it. They studied 3 patients with pityriasis rubra pilaris and demonstrated that each had impaired dark-adaptation, a finding considered diagnostic of vitamin A deficiency in the absence of organic eye disease. One patient had been subjectively aware of night blindness. Inadequate diet did not appear to be the responsible factor. On massive doses of vitamin A (150,000 international units daily) the impaired dark-adaptation

of 2 patients returned to normal in two to four weeks; the third case could not be adequately followed up. One patient manifested a high blood carotene. This suggests that the yellowish color of the skin noted in this disorder is at times due to carotenemia, and that impairment in utilizing carotene may be a basic factor in the pathogenesis. Continued vitamin A therapy for weeks to months resulted in a slow and definite but not complete improvement in the skin lesions. Brunsting and Sheard consider that in part, at least, pityriasis rubra pilaris may be due to a disturbed vitamin A metabolism.

O'Leary⁸⁷ believes that there are two types of pityriasis rubra pilaris. The patients in one group have a detectable night blindness and are helped by vitamin A therapy. In the other group evidence of vitamin A deficiency cannot be demonstrated and the skin lesions are not improved by vitamin A therapy. He adds, however, that the patients in the second group may have a deficiency of some other vitamin or combination of vitamins necessary for the utilization of vitamin A that has not yet been recognized. Gross^{88, 89} noted improvement in pityriasis rubra pilaris with niacin and with yeast therapy, a point suggesting a more complex deficiency than that of pure avitaminosis A or improvement in liver metabolism of vitamin A. Pettler⁸⁶ has reported patients with pityriasis rubra pilaris who responded favorably to vitamin A therapy, as have others.^{90, 91}

ICHTHYOSIS

Ichthyosis simplex is a congenital abnormality of cornification of the skin, commonly beginning months to years after birth and characterized by a dry, rough, fissured, scaly skin with diminished sebaceous-gland and sweat-gland activity, which is worse in the winter and improves in summer.⁹² It is a not uncommon condition, especially when of mild degree. A hereditary trait is frequently noted. On rare occasions the eyes are involved.⁹³

Cod-liver oil has been used empirically in the past for the treatment of ichthyosis. Sulzberger and his co-workers⁹⁴ specifically credited the improvement noted in mild ichthyosis that they treat-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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ed to the prolonged use of massive doses of vitamin A. Baer and Vogel⁹⁵ reported that 3 ichthyotic patients treated with vitamin A manifested improvement in both their skin lesions and dark-adaptation curves. This was proof that varying degrees of night blindness may occur in ichthyotic patients. Vail⁹³ noted improvement in both corneal and skin lesions of an ichthyotic patient treated with vitamins A and D. None of these papers, however, present the authors' data in detail.

Rapaport, Herman and Lehman⁹² reviewed the considerations linking ichthyosis to vitamin A deficiency. These included the following: frequent association in the same patient of both ichthyosis and the follicular keratotic lesions of avitaminosis; ichthyotic lesions on the legs of patients in published illustrations depicting the skin lesions of vitamin A deficiency; a seasonal fluctuation, with great amelioration or complete return to normalcy during the summer in both ichthyosis and the phrynoderma of vitamin A deficiency; improvement for the latter condition has been explained by the greater vitamin A content of foods during the spring and summer months; a frequent delay in the first appearance of ichthyosis until after weaning; a marked dryness of the skin in both conditions, with deficiency or absence of sweat-gland and sebaceous-gland secretions; a predilection for involvement of the same regions of the skin in both conditions; and similarity in the pathologic histology of the skin in both disorders.

Rapaport and his co-workers made an extended study of 6 patients with ichthyosis. Five who were examined by means of a photometer were found to have impaired dark-adaptation (night blindness). Both the night blindness and the skin lesions responded to vitamin A therapy—the former quite readily, the latter only after prolonged use of large doses. Improvement in the skin was striking but did not reach entire normalcy. A physician-patient who recorded careful observations manifested notable improvement on 60,000 to 100,000 international units of vitamin A daily for two years, the improvement being maintained through two winters. Treatment was then discontinued during four summer months, with recrudescence of the ichthyosis, which again responded favorably when vitamin A therapy was reinstated. This observation indicates the need for prolonged and continuous vitamin therapy in ichthyosis. Another patient did not respond to oral administration of vitamin A, but improved considerably with intramuscular injections of 100,000 international units of this vitamin 3 to 4 times weekly for several months. The intramuscular preparation contained practically no vitamin D, thus excluding the possibility

that the vitamin D present in most fish-liver-oil concentrates was responsible for the favorable response to oral therapy in some patients. This parenteral response suggested defective absorptive of vitamin A from the gastrointestinal tract. However, Rapaport et al. emphasize that there are "many possible disturbances in the chain of vitamin A metabolism, which begins with ingestion at one end and progresses through digestion, absorption, conversion, storage, transportation and so on to finally, at the other end, utilization of the vitamin A by the retina and other epithelial tissues." The mechanism of vitamin A deficiency might function anywhere along this chain, and might even vary from patient to patient. The hereditary mechanism so often present in ichthyosis is explained by Rapaport et al. as possibly one of inheritance of some disorder of vitamin A metabolism rather than one of a direct inheritance of the abnormal skin. In other words, the patient develops ichthyosis because he inherited the inability properly to absorb or metabolize vitamin A.

It should not be overlooked that an ichthyotic-like skin may occur in chronic pellagra. Field and his co-workers⁶⁸ have published an excellent illustration of this lesion. Since the skin in Rapaport, Herman and Lehman's⁹² patients did not become entirely normal, it is possible that some nutritional factor other than vitamin A plays an accessory but probably lesser role in its etiology.

SJÖGREN'S SYNDROME

Sjögren⁹⁶ in 1933 described the eye disorder and the commonly associated mucous membrane changes now known as Sjögren's syndrome. A similar clinical syndrome has also been described by Jonathan Hutchinson.⁹⁷ Dryness of the skin and mucous membranes resulting from deficient secretion of the glands, particularly the lacrimal, salivary, upper-respiratory and sweat glands, and the glandular apparatus, characterizes this disorder. Keratoconjunctivitis sicca, xerostomia, rhinopharyngotracheobronchitis sicca with impairment of the act of swallowing and of the olfactory and gustatory senses, deficient sweating, achylia gastrica and various other symptoms result from the deficient secretion of these glands. The syndrome occurs most commonly in women of postmenopausal age. Chronic polyarthritides exists in many cases. Bilateral parotid-gland swelling, sometimes remissive and occasionally persistent, may follow the xerostomia.⁹⁸⁻¹⁰¹ In a general sense, the name "Sjögren's syndrome" appears to be applied to the symptom complex of dryness of the cornea and conjunctivas and of the oral and upper-respiratory mucous membrane, with or without an associated enlargement of the

parotid glands. Keratoconjunctivitis sicca is more commonly present alone than with the entire syndrome. Bruce⁹⁸ reported 14 cases seen in New York City; only 4 had the complete syndrome.

Stahel⁹⁹ considers Sjögren's syndrome a manifestation of vitamin A deficiency with resultant disturbances in ectodermal and endodermal tissues. He treated a patient with vitamin A over a period of months, with striking improvement. The olfactory and gustatory functions became normal, swallowing became easier, sweating returned, and the conjunctivas returned to normal. In Sutton and Sutton's¹⁰² textbook of dermatology Sjögren's syndrome is classified etiologically as avitaminosis A. Sulzberger¹⁰³ noted that a patient with Sjögren's syndrome improved with vitamin A therapy, but not with most other vitamins or with iron therapy. Dryness of the corneas and conjunctivas has long been considered a manifestation of vitamin A deficiency. In this condition it appears to result from diminished lacrimal secretion. That the same deficiency may be a cause of the other features of this syndrome apparently represents a new opinion. The few successful therapeutic reports mentioned are at least suggestive of its validity. A final opinion awaits additional studies. Although Sjögren's syndrome is not predominantly one of the skin, mention of it is made here to stress the widening concept of clinical disorders attributable to avitaminosis A.

MISCELLANEOUS CONDITIONS ATTRIBUTED TO VITAMIN A DEFICIENCY

In addition to the previously mentioned disorders, which have already been reported frequently enough to justify their receiving significant attention, there are a number of isolated reports of miscellaneous conditions. These warrant consideration because they all seem to point to a common denominator.

Sulzberger and his associates, Goodman, Kanof and Baer,^{94, 104} used large doses of vitamin A varying from 30,000 to 500,000 U.S.P. units per day over periods of several months, with improvement in cases of dryness of the skin, mild ichthyosis, keratosis pilaris and brittleness of the nail. They also noted with the same therapy that in some cases of dryness and brittleness of the hair the latter resumed a normal sheen and appearance.

Goodman¹⁰⁴ thinks that vitamin A deficiency can produce a picture which is like pseudopelade. Of 10 patients seen by him, all but 1 had keratosis pilaris associated with the scalp lesion. He did not expect the atrophic area of the scalp to respond to vitamin A therapy, but noted definite

improvement in the lesions elsewhere on the body.

Sulzberger and his co-workers^{94, 104} noted similar results for lichen spinulosus with folliculitis decalvans, a scalp disorder resembling pseudopelade in its end result, patchy atrophy, but differing from pseudopelade in that it presents in its active stages a pronounced element of follicular inflammation including pustulation. Garfield¹⁰⁵ used vitamin A therapy for 2 patients with lichen spinulosus with good results.

The similarity of the histology of the lesions in keratosis blennorrhagica (the dermal syndrome seen occasionally in patients with gonococcal infection, particularly when systemic and severe) with those of keratosis follicularis of avitaminosis A led Combes and Behrman¹⁰⁶ to study the effect of vitamin A therapy on this skin eruption. There was a striking improvement in the skin lesions of their patient after other forms of therapy had failed. They raised the question whether keratosis blennorrhagica might not occur in patients with gonorrhea who had in addition some disturbance in vitamin A metabolism. This point obviously cannot be settled by a single favorable case report, and confirmation is awaited.

Straumfjord¹⁰⁷ has presented preliminary observations suggesting that vernix caseosa may be a manifestation of vitamin A deficiency in the newborn. He questions whether vernix caseosa is a normal substance because many normal babies are born with none. Its occurrence on the palms and soles seems to rule out its derivation from the sebaceous glands. Twenty-five women received up to 100,000 U.S.P. units of vitamin A through six months of pregnancy. Twenty-one had babies with little or no vernix, and only 4 had babies with moderate or much vernix. Thirty-one women received no additional vitamin A other than what their diet contained. Twenty-three of these had babies with moderate or much vernix. This interesting report awaits confirmation by others.

Mandelbaum and Schlessinger¹⁰⁸ proved that vitamin A could be absorbed through the intact human skin in physiologically significant quantities, their evidence being the restitution toward normal of dark-adaptation curves in night-blind subjects experimentally deficient in vitamin A when the ointments containing vitamin A were rubbed into the skin. They suggest this as an alternative route to parenteral injection when intestinal absorption is impaired, and think that the specific cutaneous lesions of vitamin A deficiency may respond favorably to this form of therapy. The favorable report by Baer and Vogel,⁹⁵ who used a vitamin A ointment in the treatment of dry skin and ichthyosis, supports this contention.

The rapidly increasing number of conditions— all characterized by abnormalities of keratization of the epithelium of the skin—for which vitamin A therapy has proved helpful or curative suggests that ideas concerning what constitutes vitamin A deficiency are undergoing some remarkable changes. "Dysvitaminoses" as postulated by Sulzberger and Cope^{109, 110} to indicate abnormal conditions of demand, utilization and transport of vitamins may prove to be more important and prevalent for vitamin A than the simple dietary deficiency of this vitamin stressed so much in the literature of the last few years.

In summary, it should be recalled that skin lesions attributed to vitamin A deficiency for the most part respond slowly to therapy and require large doses (50,000 to 200,000 or more U.S.P. units per day) for months and perhaps years. Large doses of vitamin A may be required continuously to maintain improvement. Oral therapy is not always efficacious, the parenteral route at times being required. The deficiency in many cases seems to depend on abnormal metabolism by the body rather than on a deficient diet. A familial tendency to inherit this abnormality of vitamin A metabolism appears to be not uncommon. Blindness is rarely a subjective complaint; a dark-adaptation test is usually necessary to elicit its presence, and it may be completely absent although the skin lesions are of marked degree. Xerophthalmia of severe degree appears to be uncommon. The mechanism responsible for the many different patterns that an end organ such as the skin may manifest in response to the same vitamin deficiency is not clear. The entire group of disorders characterized by abnormalities of keratosis appears one for much promising research.

CHEILOSIS AND ANGULAR STOMATITIS

Observations by Stannus¹¹¹ in 1912, and later by others, suggested a nutritional disturbance as a cause of various changes in the lips that have been called cheilosis or cheilitis. To Sebrell and Butler¹¹² goes the credit for the demonstration that it may occur in riboflavin deficiency. This they accomplished by demonstrating its development in subjects with experimentally produced riboflavin deficiency and its specific subsidence when riboflavin was added to the diet. Sydenstricker,¹¹³ Spies¹¹⁴ and Jolliffe,¹¹⁵ with their co-workers and others, confirmed and extended Sebrell and Butler's observations. I¹¹⁶ have elsewhere reviewed in detail the clinical picture of riboflavin deficiency.

The recent literature indicates that the relation of cheilosis to ariboflavinosis is not so clear-cut as was originally believed. Smith and Mar-

tin¹¹⁷ noted its disappearance in 3 patients with pyridoxine therapy. Hou¹¹⁸ suggested that ariboflavinosis together with an associated subclinical deficiency of niacin is required to produce marked degrees of cheilosis. Machella¹¹⁹⁻¹²⁰ has considered this subject in detail. He studied patients with cheilosis who manifested no other features of the ariboflavinosis syndrome and who did not respond to riboflavin. He concluded that cheilosis is not always due to riboflavin deficiency alone. It may occasionally respond to pyridoxine or niacin, or may require the entire vitamin B complex in the form of yeast or liver extract. He noted further that hemorrhagic cheilosis may respond only when ascorbic acid is added to the therapeutic regime. Both pyridoxine and pantothenic acid have been suggested as necessary for the proper metabolism of riboflavin, thus affording a possible explanation of the inconstant response of cheilosis to riboflavin therapy.

There are many other causes of changes in the lips¹²¹⁻¹²³ besides vitamin deficiency, as a glance through any standard dermatology book or the *Quarterly Cumulative Index Medicus* will reveal. Sulzberger and Goodman¹²⁴ emphasize the importance of sensitivity to lipstick as a cause of cheilitis in women. When isolated cheilitis in a woman is seen, this possibility must certainly be considered. Sensitivity to dental plates,¹²⁵ chewing gum,¹²⁶ toothpaste,¹²⁷ mouthwashes,¹²¹ cigarette-holders,¹²¹ throat lozenges,¹²⁸ the reed used in the mouthpiece of a musical instrument¹²⁹ and other agents have been reported as causing cheilitis. Exposure to sun, even in men, may produce cheilitis.¹³⁰ In women, it may exacerbate or initiate sensitivity to lipstick. Cheilitis is considered by some as part of the Plummer-Vinson syndrome.¹³¹

An early lesion in riboflavin deficiency is accretion at the commissures or angles of the mouth, which may result in superficial transverse fissuring, resembling the perlèche so well known to the dermatologist. This characteristic lesion has been referred to as the angular stomatitis of Stannus and as Sebrell's lesion. It may precede or accompany changes in the lips (cheilosis).

The resemblance of nutritional angular stomatitis to the dermatologic entity perlèche has not gone unnoticed. Sulzberger and Cope¹⁰⁹ believe them to be distinct disease entities. Sutton and Sutton¹³² stress the frequency of perlèche in childhood and also the commonness with which various bacteria and fungi can be isolated from this lesion. Spies and his co-workers¹¹⁴ found nutritional angular stomatitis to be as frequent in children as in adults, and furthermore readily

tured *Staphylococcus aureus* or *Streptococcus haemolyticus* from the fissures in most cases. They found that infection subsided spontaneously without chemotherapy as the fissures healed with nutritional therapy. The likelihood that the infection of perlèche is related to ariboflavinosis in a manner analogous to the fusospirochetosis of pellagrous stomatitis has been discussed by Sutton and Sutton. The striking therapeutic success noted by Spies and his co-workers¹¹⁴ appears to give some weight to the Suttons' contention.

Unfortunately, not all commissural fissures are nutritional—a situation more evident in private practice than in the clinic. Labial fissures may follow trauma from manipulations about the lips by a dentist. Weisberger¹³³ has noted angular fissures to be common in persons with ill-fitting dentures, due no doubt to the constant drooling of saliva that resulted. The fissures showed no improvement following treatment with riboflavin or vitamin B complex, but responded readily when the dentures were changed so as to eliminate the drooling. Ellenberg and Pollock¹³⁴ have likewise been impressed with the importance of poorly fitting dentures in causing angular fissures. They emphasize the frequent association of glossitis with the labial lesions. They call the syndrome "pseudo-ariboflavinosis." Suitable dental treatment is recommended.

PURPURA OF VITAMIN-DEFICIENCY ORIGIN

Vitamin C, vitamin K and probably vitamin P deficiency produce a hemorrhagic diathesis. The differences and similarities in the dermal manifestations of the purpura in these three deficiencies will be briefly reviewed. Other aspects of their hemorrhagic diathesis will not be considered. It should not be overlooked that many causes for purpura other than these deficiencies exist.

Vitamin K Deficiency

The importance of vitamin K as a precursor for the formation of blood prothrombin and the maintenance of normal hemostasis is now well known, as is the frequency with which purpura due to vitamin K deficiency occurs in obstructive jaundice, biliary fistula, liver disease, sprue, chronic diarrhea and high fever and in the newborn.

Bacterial synthesis of vitamin K in the intestinal tract probably accounts for the rarity of hypoprothrombinemia arising solely from a deficient diet. A few probable cases have, nevertheless, been reported. Kark and Lozner¹³⁵ studied, under controlled conditions, 4 patients with a mild degree of hypoprothrombinemia; they had multiple nutritional deficiencies but not liver or intestinal disease. Their prothrombin levels returned to

normal on the administration of oral vitamin K without bile salts. Scarborough¹³⁶ made a similar study of 18 nutritionally deficient patients. He emphasized that nutritional hypoprothrombinemia could be demonstrated by the dilution method for prothrombin of Kark and Lozner but not by the Quick technic. In none of these cases was the prothrombin low enough to have caused bleeding. Aggeler, Lucia and Fishbon¹³⁷ report the case of a thirty-two-year-old woman with severe anorexia nervosa with purpura. Her prothrombin concentration by the Quick method was 15 per cent. No organic liver or intestinal disease was present. The purpura did not respond to ascorbic acid, but did to vitamin K, with a resultant rise in prothrombin concentration. This case appears to be an exception, but the circumstances were extreme.

It must be extremely rare for deficiency of vitamin K in the diet alone to cause purpura. Nevertheless, it may assume importance when additive to other factors interfering with normal vitamin K metabolism.

Skin purpura in vitamin K deficiency may be striking. Ecchymoses and suffusions of blood are common, and may at times cover large areas of the skin.¹³⁸ They are especially prominent over pressure areas and lack the orthostatic tendency common in scurvy. Subcutaneous hematomas or ecchymoses about needle punctures in the antecubital fossa or ear lobe are frequent, a diagnostic point emphasized by Kark and Souter.¹³⁹ Generalized petechial hemorrhages and perifollicular hemorrhages on the extremities do not occur.^{138, 140} "Bleeding may occur from the gums after slight trauma, but the gums themselves do not show the purple sponginess characteristic of scurvy."¹³⁸ The bleeding time is usually normal and capillary fragility is unaltered.¹³⁸ Diagnosis depends on a diminished prothrombin level in the blood and the characteristic response to vitamin K therapy.

Vitamin P Deficiency

Szent-Gyorgi in 1936 postulated the existence of vitamin P, a flavone substance, so named because it regulated capillary permeability. It has been prepared in relatively pure form as citrin, which consists of at least two substances of the benzopyrone type—hesperidin and demethylated hesperidin (eriodictyol glycoside or eriodictitin), the latter probably being the more active form.¹⁴¹ There has been considerable controversy concerning the exact chemical nature of vitamin P, the capillary-permeability specificity claimed for it, the ability to produce its deficiency experimentally in animals and the therapeutic results claimed for its clinical use.

Lindheimer, Hinman and Halliday¹⁴¹ in a recent paper critically reviewed the now rapidly expanding controversial literature on this subject. In the part of their conclusion that is of clinical import they state, "Human clinical studies show that citrin has a definite effect in improving low capillary resistance in various conditions, whether of known dietary origin or not." Zacho,¹⁴² Ruszyński and Benko¹⁴³ and Bacharach¹⁴⁴ all report the production of lowered capillary resistance in guinea pigs and rats receiving a scorbutogenic diet containing large daily doses of pure ascorbic acid but lacking in vitamin P. Treatment of these deficient animals with citrin but with no other change in the experimental setup resulted in restitution of capillary fragility to normal over a period of days.¹⁴⁵

The papers by Kugelmass,¹⁴⁶ Jersild,¹⁴⁶ Scarborough,¹⁴⁷ Rapaport,¹⁴⁸ and others are typical of those reporting worthwhile therapeutic results in clinical practice. Jersild suggested that Schönlein-Henoch's purpura may be due to vitamin P deficiency. Scarborough found vitamin P useful in the treatment of purpura senilis. The valid criticism that treatment of clinical patients is difficult to control and evaluate seems effectively answered by Scarborough, who not only produced isolated P avitaminosis in man but has also attempted to delineate a specific clinical picture for it.

Two experimental subjects suffering from nutritional deficiency were placed for several months on a vitamin-free diet, supplemented by chemical vitamins including large doses of ascorbic acid but no vitamin P. There was a progressive increase in capillary permeability, and petechial hemorrhages appeared on the legs (orthostatic), in pressure areas and after the application of a tourniquet. Various symptoms were noted. The large subcutaneous hemorrhages or bleeding gums seen in scurvy did not appear. Institution of vitamin P therapy relieved the symptoms within forty-eight hours, no further petechial hemorrhages developed, and the capillary resistance progressively returned to normal. The course of the experiment, the findings and the response to therapy were similar in both subjects. This ingenious experiment, although apparently conclusive, awaits confirmation. Scarborough also treated several scorbutic patients under similar controlled conditions, giving vitamin P but withholding vitamin C, with similar improvement in capillary resistance. He concluded that "administration of vitamin P can produce an increased capillary resistance in the scorbutic subject either before or after treatment with ascorbic acid."

Scarborough noted circumpilar (perifollicular) petechial hemorrhages in his pure vitamin P-

deficient subject, thus questioning the specificity of this finding for the clinical diagnosis of scurvy. Except for a positive test for lowered capillary resistance and a slightly increased bleeding time (Duke¹⁴⁹), an exhaustive hematologic investigation of the two experimental subjects was entirely normal.

The clinical picture of avitaminosis P as postulated by Scarborough is one of much decreased capillary resistance, petechial hemorrhages, spontaneous or over pressure areas (being at times circumpilar in location), a slightly prolonged bleeding time (Duke) and varying subjective symptoms, such as pain in the legs on exertion, pain across the shoulders, weakness, lassitude and fatigue, all responding to specific vitamin P therapy. Scarborough adds that since the exact chemical nature of vitamin P used by him is still unknown, its therapeutic use should be limited to experimentally controlled conditions.

Vitamin C Deficiency

That the concept of scurvy has its roots in antiquity is clearly shown in the excellent reviews by Ralli and Sherry¹⁵⁰ and Faulkner.¹⁵¹ The purpuric manifestations commonly considered diagnostic of scurvy are based on the study of the disease as seen in the clinic or in private practice, the descriptions not varying widely over the years. It is a truism that a pure vitamin deficiency is a rarity in clinical practice, and the scorbutic patient as ordinarily seen is very likely to have some associated nutritional disturbance. It is worthwhile, therefore, to review the type of purpura seen in scurvy when other deficiency factors are known and controlled.

The classic experiment by Crandon, Lund and Dill,⁶⁶ in which Crandon lived for six months on an experimentally controlled diet deficient only in vitamin C, with resultant production of pure scurvy, serves as the keystone for analysis of this question. A significant number of moderate-sized perifollicular hemorrhages occurred, which did not fade on pressure and were not elevated, appearing first on the lower leg and then on the thighs (an illustration of them appears in their paper). An orthostatic tendency was demonstrated, since they were numerous when Crandon was on his feet for several hours. The experiment did not continue long enough to produce gross ecchymosis of any degree. The gums were essentially nonhemorrhagic, relatively firm and not "heaped up." The Gothlin, Dalldorf and Rumpel-Leeds tests were negative, indicating normal capillary resistance. The Ivy bleeding time remained normal throughout. Other hematologic data relative to hemostasis were normal. The perifollicu-

lar hemorrhages and other skin manifestations cleared promptly on institution of vitamin C therapy.

The lack of bleeding spongy gums in scorbutic infants before eruption of the teeth and in scorbutic adults who are edentulous is well known. Crandon's experiment indicates that bleeding gums in scorbutic adults may likewise be absent if the teeth and gums are otherwise healthy before the deficiency commences. The heaped-up, spongy, bleeding, purplish gums so common in clinical scurvy probably represent vitamin deficiency in addition to pre-existent gingival and dental disease. Although the gums may bleed in vitamin K deficiency when traumatized and more rarely spontaneously, they are never purplish, spongy or swollen as in scurvy.¹³⁸ According to Scarborough,¹⁴⁹ the gums were normal in his patients with avitaminosis P.

This experiment indicates that the capillary-fragility test may be normal during frank scurvy. If the concept of capillary permeability control by vitamin P is true, it would further indicate that Crandon did not have an associated vitamin P deficiency with his scurvy. Rapaport¹⁴⁸ lists six groups of investigators who were unable to correlate increased capillary fragility with states of vitamin C deficiency. Yet a positive tourniquet test with production of showers of petechiae is often seen in frank clinical scurvy.

Except under very special circumstances, Scarborough¹⁴⁷ has not found ascorbic acid capable of increasing capillary resistance. Extravascular suffusion of blood into the tissues, whether occurring in the course of the disease or produced artificially, has been found temporarily to increase capillary resistance in clinical scurvy, which he considers a "complex deficiency state."¹⁵² This observation incidentally affords some rationale for the common empirical practice of injecting intramuscularly some of the patient's own whole blood for various hemorrhagic disorders.

Davidson¹⁵³ kept 2 scorbutic patients on a vitamin C-free diet under controlled conditions. Therapy with crude vitamin P (assayed to demonstrate the absence of vitamin C) restored the tourniquet test to normal, but had no effect on the perifollicular hemorrhages and ecchymosis of the legs. The latter cleared only with vitamin C therapy. Scarborough¹⁴⁷ has reported several similar experiments, as have Cameron and Mills.¹⁶⁴ Levkowich and Batchelder¹⁵⁵ report that 2 girls kept on a scurvy-producing diet supplemented with crystalline ascorbic acid manifested petechiae that became less prominent when "natural sources" of vitamin C were substituted for the crystalline ascorbic acid.

The specificity of perifollicular hemorrhages for scurvy seems questioned by Scarborough's observation that circumpilar petechiae (evidently the same thing) appeared in his 2 patients with supposedly pure vitamin P deficiency. As mentioned before, his experiments are still unconfirmed. It appears that ecchymoses and other soft-tissue bleeding are the most characteristic purpuric manifestations of true scurvy.¹⁴⁹

Table 3 summarizes the pertinent features of the purpuras associated with deficiencies of vitamin K, vitamin C and vitamin P in human beings and is based on data available in the literature. These differential features must for the present be considered as only tentatively correct, since they depend in part on a number of unconfirmed observations.

PALMAR ERYTHEMA

Perera¹⁵⁶ describes palmar erythema as "a symmetrical, erythematous, capillary and arteriolar dilatation involving the eminences of the palms and the digits of the hands, rarely the soles, at times extending over the fingertips to the nailbeds and lateral distal phalanges." It has the appearance of a diffuse or blotchy redness. In milder stages the palmar eminences alone may be involved. The erythema blanches on pressure and the skin feels warmer to touch than usual. Walsh and Becker¹⁵⁷ and Bean^{158, 159} have reviewed this subject in detail. Their papers contain excellent illustrations of palmar erythema.

Because of its frequent presence in persons with portal cirrhosis, palmar erythema has been called "liver palms."¹⁶⁰ It also occurs in pregnancy^{156, 157, 159, 161} and in a miscellaneous group of conditions most of which are characterized by malnutrition.^{156, 159} Associated signs of deficiency, such as cheilitis, glossitis and peripheral neuritis, have been noted in some patients.¹⁵⁶ The not uncommon association of spider angiomas and palmar erythema in the same person has been emphasized by Walsh and Becker¹⁵⁷ and Bean.¹⁵⁹ The disease may occur in normal persons but is rare.

Perera¹⁵⁶ considers the cause obscure, but stresses its common association with chronic disease and prolonged dietary insufficiency or deficiency states. He reports that intense multiple-vitamin therapy did not generally relieve it, which has been my experience at Boston City Hospital.

Bean¹⁵⁸ believes that palmar erythema may result from abnormal metabolism of the 17-ketosteroid hormones. He produced not only palmar erythema but also spider angiomas following administration of potent estrogens to a patient with cirrhosis. On discontinuance of the estrogens both conditions gradually disappeared. In a more re-

DIFFERENTIAL FACTORS	VITAMIN K DEFICIENCY*		VITAMIN C DEFICIENCY		VITAMIN P DEFICIENCY
	LATENT HEMORRHAGIC HYPOPROTHROMBINEMIA (CAUSING ONLY ATRIAL THROMBOSIS)	SPONTANEOUS HEMORRHAGIC HYPOPROTHROMBINEMIA (SPONTANEOUS BLEEDING)	Dietary deficiency	Orthostatic in legs from pressure or trauma to skin, may also appear spontaneously without obvious trauma	Dietary deficiency
Chief reason for development of the vitamin deficiency	Liver disease obstructive jaundice, sprue, diarrhea, high fever, infancy (newborn) and so forth	Liver disease, obstructive jaundice, sprue, diarrhea, high fever, infancy (newborn) and so forth			
Factors conditioning the appearance of the purpura	At sites of obvious trauma such as recent wounds, lacerations, traumatic and so forth, interdigital ulcers (ulcerative colitis), needle puncture areas of skin, vigorous brushing of teeth and so forth	Appears spontaneously, with little or no trauma. In skin, aneurysm, membranes, brain, uterus and so forth			Orthostatic in legs may appear spontaneously or follow pressure on the skin
Dermal manifestations of the purpura	At above needle puncture ecchymosis or thrombosis the most characteristic skin lesion in the average patient, no petechiae	Ecchymoses and effusions of blood in skin, especially over pressure areas, skin purpura and always a prominent feature, may be localized although petechious internal bleeding is present, no petechiae			Petechiae the chief lesion, may be spontaneous or appear over pressure areas, may be perifollicular in location
Spontaneous mucous membrane bleeding	Absent	Present			Absent
Gums	Normal no bleeding except from trauma	Gums relatively normal in appearance, may show ecchymosis and bleed spontaneously but are not heaped up, spongy or purplish			Normal
Perifollicular localization of hemorrhagic diathesis	Absent	Absent			Present
Blood prothrombin level	Below 35 per cent of normal	Below 20 to 15 per cent of normal			Normal
Clotting time	Generally normal	Commonly prolonged			Normal
Not retraction	Normal	Normal			Normal
Jaundice and white cell platelet vitamin C content	Normal	Normal			Normal
Bleeding time (Duke)	Normal at the time of test, bleeding may occur from the puncture wound after an interval of time	Usually normal occasionally prolonged bleeding may occur from the puncture wound after an interval of time			Slightly prolonged
Platelet count	Normal	Normal			Normal
Toursiquet test (Pumpkin-seed extract) bleeding of a torn piece of the arm	Normal	Normal			Normal
Comment	A slight diminution of the prothrombin content of the blood may result from a pure nutritional deficiency of vitamin K, but probably never or only rarely will it be of a degree sufficient to cause bleeding; it may however be additive to the causes listed above	Scurvy as seen clinically may represent varying combinations of the features of both these deficiencies			Strongly positive, many petechiae appear below level of the tourniquet

*Based on Kark and Souder's¹⁴ classification of hypoprothrombinemia

¹⁴C. S. Davidson: Personal communication

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29221

PRESENTATION OF CASE

A forty-nine-year-old man, a grocery clerk, entered the hospital because of crampy abdominal pain.

Two months prior to admission the patient had "bronchitis," from which he never fully recovered as a slight cough persisted. Eight days before admission he developed a slight head cold and that evening took two tablespoonfuls of Epsom salts, although his bowels had always been regular. He was awakened at 5:00 a.m. with sharp, crampy, "agonizing" pains in the abdomen that intermittently occurred throughout the day at ill-defined intervals and gradually localized in the right side of the abdomen. After three days he felt better, but three days prior to admission the pain returned and seemed to localize in the right upper quadrant. On the day before admission his physician found a "mass" in the right side. At no time was there any nausea, vomiting, gas, anorexia, chills, fever, change of bowel habits or bloody, tarry or acholic stools. For many years the patient had had nocturia (two to four times) without any other urologic symptoms. During the present illness he had lost 10 to 15 pounds, which he attributed to a "light diet."

The family and past histories were noncontributory.

Physical examination revealed a well-developed and well-nourished man who complained of sharp pains in the right upper quadrant but who did not appear to be uncomfortable. The chest was hyperresonant. The heart and lungs were normal. There was slight tenderness in the right side of the abdomen at the level of the umbilicus, where a grapefruit-sized mass was easily felt, which moved slightly with respiration but did not seem to be attached to the liver. The surface markings and consistence of the mass could not definitely be made out. No other masses were felt. The prostate was slightly enlarged, soft and nontender.

The blood pressure was 145 systolic, 80 diastolic. The temperature was 101°F., the pulse 84, and the respirations 20.

*On leave of absence.

Examination of the blood disclosed a white-cell count of 12,000. The urine was acid in reaction, had a specific gravity of 1.015, and gave a + test for albumin; the sediment contained 15 white cells per high-power field. A stool was guaiac negative. The blood Hinton test was negative. The blood protein was 4.5 gm. per 100 cc., and the chloride 99.7 milliequiv. per liter; the prothrombin time was normal.

A flat plate of the abdomen showed normal kidneys. The psoas contours were not remarkable. No abnormal soft-tissue mass was observed. Intravenous pyelograms showed rapid filling of the pelves and calyces on both sides, without evidence of distortion. The bladder was normal. A barium enema passed readily from the rectum to the cecum, outlining a normal sigmoid and descending and transverse colon. In the ascending colon on the lateral wall, extending from a point 6 cm. above the tip of the cecum upward for a distance of 8 cm., was a lobulated filling defect that had the appearance of an intrinsic lesion. There was no evidence of obstruction.

On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. HORACE K. SOWLES: There seem to be a few red herring scattered along this trail. We have a history of "bronchitis" two months prior to entry, which never cleared up, and eight days before entry the patient had a head cold with a temperature of 101°F., not to mention the white-cell count of 12,000 and the 15 white cells in the urine, a picture that perfectly well goes with renal infection, such as pyelonephritis, pyonephrosis or perinephritic abscess. X-ray studies, however, showed that the kidneys were normal and that the psoas muscle was clear. So we can rule out perirenal abscess or mass, and that gives the kidneys on the whole a relatively clean bill of health.

Then we come to the x-ray films of the bowel, which show definite pathology—a fairly large intrinsic tumor of the cecum protruding into the bowel cavity. The tumor was lobulated and, I should say from the description, not ulcerative. If this tumor were ulcerated, that might explain some of the other symptoms, such as the high white-cell count and the fever, but one would also expect guaiac-positive stools, which were not recorded. With an ulcerated tumor of the cecum one usually finds a definite blood picture in the form of anemia, but there was no evidence of that. The x-ray film points to a nonulcerating lesion, which Dr. Holmes will tell us more about.

DR. GEORGE W. HOLMES: In this film the kidneys are fairly well seen. They do not appear to

be large or abnormal in shape. The calyces are also quite clearly made out, and I should say they are within normal limits. In other words, x-ray

cecum but not producing obstruction of any kind. The man who did the examination had the advantage of being able to palpate the patient, but



FIGURE 1.

examination is negative so far as kidney disease is concerned.

The psoas muscle shows up quite well. The statement about the soft-tissue mass can be interpreted in two ways. I presume that they meant that they did not see a mass on the films, not that it was overlooked. I certainly do not see anything characteristic of a soft-tissue mass in the abdomen, although apparently it was felt.

As one reads the report on the gastrointestinal examination one gets a different idea from that obtained by looking at the films. Certainly this is not the characteristic angle of deformity that is seen in carcinoma of the colon. This film (Fig. 1) appears to bring out the lesion as well as any. There seems to be a mass of considerable size along the outer margin of the bowel, just above the cecum, perhaps extending into the

my impression is that the mass is extrinsic and perhaps adherent to the wall of the bowel rather than within it.

DR. SOWLES: This mass was in the right upper quadrant, moved with respiration and was not attached to the liver; all this fits in with a kidney mass, presumably inflammatory because of the fever, elevated white-cell count and pus cells in the urine. The various x-ray studies rule out the kidney quite well, but this reasoning may fail us. If the mass is extrinsic, it may be an inflammatory mass associated with infection in the renal tract on the right side, but aside from that one must explain the story of pain that the patient had when he took Epsom salts. Perhaps they were just cramps due to Epsom salts. If the patient had a large lobular pedunculated mass in the cecum, the stress of the salts he may have devel-

oped intussusception, which may cause crampy pains. I cannot combine the two things. Dr. Holmes, did you say that the lesion was non-ulcerative?

DR. HOLMES: I cannot tell. The cecum is not emptied, hence it is impossible to see the mucosa.

DR. SOWLES: I cannot see how a nonulcerative tumor in the wall of the cecum could have been responsible for the elevated white-cell count and fever. The patient may have had a little hang-over from the bronchitis and head cold of only eight days before. My translation of the reports of the studies on the kidneys rules them out, and from the x-ray diagnosis I should say, that this was a tumor in the wall of the cecum. Dr. Holmes suggested that it may have been extrinsic, a lobulated polypoid growth protruding into the cecum from the lateral wall. I cannot match up the two pictures sufficiently to come to a more definite diagnosis than that.

DR. FLETCHER H. COLBY: Could this have been an appendiceal abscess?

DR. SOWLES: The lesion was several inches above the tip of the cecum. Of course, one should always think of an appendiceal abscess, because one originating from the tip of a retrocecal appendix could be so located that it would press on the outer side of the cecum.

DR. G. G. SMITH: At this distance it almost looks like a soft-tissue mass opposite the second and third lumbar vertebrae.

DR. SOWLES: It does not interfere with the course of the ureter. The edge of the psoas muscle is quite clear.

DR. SMITH: Yes, but over that area it is dimmed a little.

DR. SOWLES: It could perfectly well have been an appendiceal abscess lying on the outer side of the cecum.

A PHYSICIAN: Could a large distended gall bladder produce that picture, Dr. Holmes?

DR. HOLMES: No.

DR. SOWLES: A large distended gall bladder is often low down on the right side.

DR. ARTHUR W. ALLEN: But not behind the colon.

DR. SOWLES: No.

DR. ALLEN: This man came in with what we believed to be an inflammatory mass. There was not much doubt in our minds that it was inflammatory, and since it was in the flank, we thought of kidney and also considered other possibilities, particularly acute appendicitis with abscess formation. The X-ray Department made a diagnosis of an intrinsic lesion in the ascending colon. If this was carcinoma of the ascending colon, we decided that it had perforated and that

we were dealing with a perforation with abscess formation. We kept the patient on the ward for about a week; and he improved considerably and the mass was reduced somewhat in size.

We operated under the diagnosis of carcinoma of the ascending colon with perforation, and did a preliminary ileotranscolostomy preparatory to a resection of the whole segment. When the abdomen was opened there was evidence of a good deal of inflammatory reaction. There were obvious fibrin deposits on the small intestine here and there, but we have learned that we must not touch the original lesion by palpation if we are going to do a preliminary ileotransverse colostomy, so this was not handled in any way. The terminal ileum, about 25 cm. from the ileocecal valve, was anastomosed to the midtransverse colon. The patient did well, and three weeks later we proceeded to expose the right abdomen through a separate incision, finding that the primary lesion was an appendiceal abscess, the appendix being turned on itself and occupying the retrocecal position seen in the x-ray films. We removed the appendix,—the abscess was almost completely absorbed by that time,—and the man made a perfectly good recovery.

We have been faced with this situation four or five times, and in at least two of the cases we could not tell until we had resected the right colon that the origin was appendiceal. In this man it was easy enough to determine the true diagnosis as soon as the lateral wall of the cecum was freed. The appendix was obviously the source of the mass and one could easily identify it as being in the subacute stage.

DR. SOWLES: Did you take down the ileotransverse colostomy?

DR. ALLEN: No. There was residual infection in the region, and I believe it was best to let him keep the ileotransverse colostomy. I doubt that it will trouble him in the future.

CLINICAL DIAGNOSIS

Carcinoma of cecum.

DR. SOWLES'S DIAGNOSIS

Carcinoma of cecum.

ANATOMICAL DIAGNOSIS

Appendiceal abscess.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Microscopic examination of the appendix showed that most of the infection had subsided; there was subacute and chronic periappendicitis with a little invasion of the wall in one spot.

CASE 29222

PRESENTATION OF CASE

A forty four-year-old plumber entered the hospital because of intermittent periods of constipation associated with "abdominal distress and nausea"

Approximately ten years prior to admission the

tracted pleurisy during the summer, which lasted several months and was relieved only by immobilizing the chest with adhesive strapping. There was no history of hemoptysis, night sweats, chills or weight loss.

Physical examination disclosed a well developed and well nourished man who seemed comfortable. The heart and lungs were normal. No abdom-

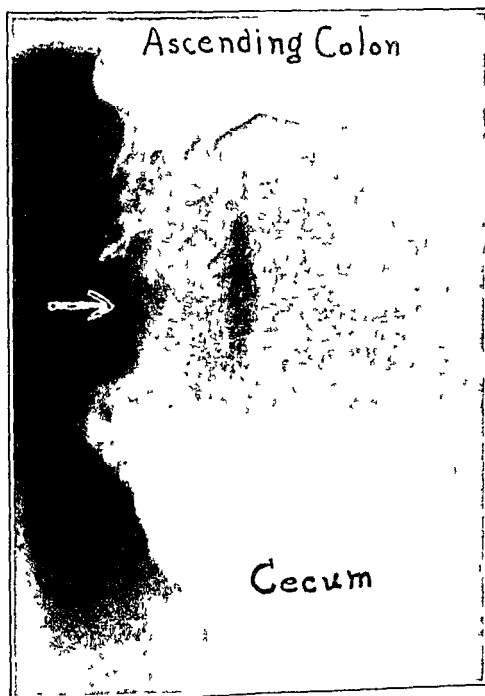


FIGURE 1

patient began to have periods of rather severe constipation that usually lasted two or three weeks and were unrelieved by enemas or cathartics. Frequently associated with the constipation were rather marked abdominal distress and nausea, but no vomiting, except immediately after the use of cathartics. There was no diarrhea, melena, hematemesis or jaundice, and the stools were of normal caliber, consistence and color.

The family history was noncontributory. For many years the patient had had frequent colds with a chronic cough during the winter. Approximately twenty years prior to admission he con-

tinued masses were felt, and no tenderness or spasm was elicited. Rectal examination was negative.

The blood pressure was 90 systolic, 58 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 14.5 gm and a white cell count of 8600. The urine was negative. A blood Hinton test was negative. The nonprotein nitrogen was 24 mg per 100 cc, and the protein 61 gm.

A barium enema revealed an area of narrowing approximately 2.5 cm in length in the ascending colon. It was about 6 cm distal to the ileocecal junction.

valve and caused considerable obstruction. The mucous membrane was not well visualized but seemed to be ulcerated. The distal margins of the lesion were shelf like, and the area of narrowing was abrupt. The cecum contained considerable fecal material, but the appendix filled rapidly. There was a small diverticulum of the ascending colon proximal to the area of narrowing, and another diverticulum in the distal transverse colon. The terminal ileum filled and appeared normal.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD L. YOUNG: Of course there are only a limited number of probabilities and various possibilities in this case. The probabilities are malignant disease, tuberculosis and diverticulitis, but from the description of the x-ray films it seems to me that the last is ruled out.

How much attention should we pay to tuberculosis? The story of pleurisy is consistent with a tuberculous infection twenty years before entry. We know that tuberculosis of the ileocecal region, where intestinal tuberculosis is most likely to be found, can occur without lung involvement. We also know that the differential diagnosis between it and carcinoma is often impossible. I do not know how much attention to pay to the attacks of severe constipation. Certainly one would not expect such attacks to have been due to malignant disease for a period of ten years. I also question whether it could have been due to tuberculosis.

When they say that the chest was normal do they mean by x-ray or merely by physical examination?

DR. BENJAMIN CASTLEMAN: By physical examination only. No x-ray film of the chest was taken before operation.

DR. YOUNG: They apparently did not take the history of pleurisy too seriously.

Then I had better make this short and say that malignant disease is the best bet. Carcinoma? Yes. But one should also remember that a lymphosarcoma is not unheard of in this area. I should pay a good deal of attention to what the roentgenologist said in describing this lesion. If the recorded description is correct, I think that tuberculosis can be discarded, and certainly diverticulitis.

I should like to get more help from the roentgenologist.

DR. LAURENCE L. ROBBINS: The area of narrowing is in the ascending colon. The only thing to suggest diverticulitis is the fact that there is a diverticulum in the ascending colon, but it is not close to the involved area. The spot film (Fig. 1) shows the upper margin of the lesion, which appears to be slightly lobulated; the area of narrowing is only about 2.5 cm. in length. The distal margin appears shelf like, but the proximal margin is funnel shaped. The area of narrowing did not appear to enlarge during examination.

I believe that the lesion was due to carcinoma or tuberculosis.

DR. YOUNG: I shall simply stick to the theory of probabilities and say that my first choice is malignant disease, with tuberculosis second. I do not believe that it makes a bit of difference so far as the patient is concerned. The only way to treat either, of course, is by resection of the right colon.

CLINICAL DIAGNOSIS

Carcinoma of cecum.

DR. YOUNG'S DIAGNOSIS

Carcinoma of ascending colon?

Tuberculosis of ascending colon?

ANATOMICAL DIAGNOSIS

Tuberculosis of cecum, with involvement of regional lymph nodes.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This patient was operated on by Dr. Robert R. Linton with a preoperative diagnosis of carcinoma of the cecum. A right colectomy and resection of a portion of the terminal ileum were performed. When opened the specimen showed an annular ulcerating lesion about 7 or 8 cm. from the ileocecal valve that measured 3 to 4 cm. in length. Microscopic examination showed it to be tuberculosis. The regional nodes also showed tuberculosis.

A point that Adams and Parsons* emphasized several years ago when they reviewed the cases of tuberculosis of the cecum at this hospital should be remembered, namely, that in cases of tuberculosis the red-cell count and hemoglobin are almost always normal or near normal, whereas in cases of cancer they are low. In this case the hemoglobin was normal.

*Adams, R., and Parsons, L. J. Tuberculosis of cecum. *New Eng. J. Med.* 224:315-319, 1941.

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THE VIRUS OF THE SO CALLED 'VIRUS PNEUMONIAS'

The primary atypical pneumonias of nonbacterial origin continue to arouse the interest of clinical and laboratory workers. A review¹ of this subject appeared in the *Journal* last year. Recent contributions bearing on the etiology of this disease are worthy of comment.

At the Rockefeller Institute, in Princeton, New Jersey, Baker² recovered from cats with pneumonia a virus that forms elementary bodies. In the form of a suspension of an infected cat's lung it readily produced typical clinical symptoms and pulmonary consolidation in mice. Baker sug-

gests that this virus may be related to the one causing some of the atypical pneumonias in man. His evidence, however, is rather tenuous. It depends in part on unpublished reports by others of cases of pneumonia occurring in places where there were sick cats, and in part on a small number of complement fixation tests performed on serums from acute and convalescent patients. The results of the latter are far from convincing.

Further observations tending to implicate cats in the transmission of certain cases of atypical pneumonia have been presented by Blake, Egan, and Tatlock.³ They observed within a brief period the occurrence of an acute respiratory disease resembling primary atypical pneumonia in members of a family and in eleven cats living in Jewett City, Connecticut. From one of the cats they recovered a virus producing a similar pneumonia in guinea pigs appeared to be more susceptible than full grown cats. Unlike that described by Baker, this one failed to infect guinea pigs also differs from most others known to cause infections of the respiratory tract, being negative, but not conclusive, evidence to indicate that the respiratory members of the family who produced the infection in it.

Still another infectious agent, isolated from cases of atypical pneumonia, was obtained from specimens of patients in autopsy pulmonary consolidation in which inoculation was obtained early in the course of the illness more recently obtained later. Similar results after inoculations in guinea pigs including neutralization tests with the cotton seed oil emulsion.

valescent serums from cases of atypical pneumonia and with serums from rabbits immunized with suspensions of human lung that had proved infectious for the cotton rat. This infectious agent, which is presumed to be a filterable virus, differs from the psittacosis-like virus that had previously been described by workers in the same laboratory. The authors consider their evidence for the causal relation of the present agent to the commoner form of atypical pneumonia to be incomplete.

Each of the agents described above is recognized by the lesions it produces in animals. Horsfall and his co-workers⁵ in the United States Naval Research Unit at the Hospital of the Rockefeller Institute for Medical Research have just described a virus recovered from patients with primary atypical pneumonia that fails to produce recognizable and reproducible infectious lesions in animals. Their agent is recognized by the fact that it stimulates antibodies in animals that are capable of neutralizing a heterologous virus, the so-called "pneumonia virus of mice." It failed to produce lesions in the lungs of mice and rats, in chick embryos and in egg membranes; nor were elementary bodies, inclusion bodies, rickettsias or bacteria recognized in tissues infected with this agent. Their virus was, however, identified as probably the same as, or closely related to, the one isolated by Weir and Horsfall⁶ in 1939 from materials obtained from similar cases after inoculation into mongooses. Evidence was also produced to show that the pulmonary consolidation in cotton rats, which they succeeded in producing by the inoculation of sputum from one of their cases, and the development of antibodies against the mouse-pneumonia virus were results of infection by one and the same agent. Serums from acute and convalescent cases of atypical pneumonia, however, failed to show an increase in neutralizing antibodies against the mouse pneumonia virus during convalescence. This failure was explained by assuming that the human antibody response was too small to be measured by the technic employed. The evidence that the Rockefeller workers have

actually obtained a virus that is etiologically related to some cases of atypical pneumonia is, at best, only remotely suggestive. Possibly they may be able to discover a more direct and a more convincing way of demonstrating its presence in cases of atypical pneumonia and its relation to the human disease.

The most exhaustive study of primary atypical pneumonia to be reported thus far has just been published by Dingle and the other members⁷ of the Commission for the Investigation of Atypical Pneumonia and Other Respiratory Diseases at Camp Claiborne, Louisiana. These workers have presented in great detail the clinical, bacteriologic and epidemiologic aspects of their cases, which on the whole were primarily of the mild variety, similar to those described in a number of previous outbreaks in schools and colleges and among hospital and military personnel. In their attempts to determine the etiologic agents in their cases, these men were aided by many of the most distinguished and experienced investigators in this field, working in different laboratories throughout the country. The results of their searches for causative agents were chiefly negative. They did, however, obtain some evidence to suggest that an unidentified agent was present in some of the cases. Repeated passages of filtered amniotic fluid from chick embryos inoculated with throat washings from certain cases resulted in the development of cloudy amniotic fluids and retardation of the growth of the embryos, with death of a considerable number. No pulmonary lesions were produced on passage of this material through mice. Specimens of sputum and throat washings from four of their patients also produced hemorrhagic lesions in the lungs of cotton rats after intranasal inoculation. No bacteria were cultured from the lesions, and the agent could be passed from one animal to the other by direct inoculation of the lung material but not with the same material after Berkefeld filtration. In occasional lesions, cytoplasmic inclusion bodies were seen. On the basis of their results, Dingle and his co-workers think it

likely that a new agent, probably a virus, was responsible for their cases of primary atypical pneumonia. The studies of this commission are now being continued at Fort Bragg, and should yield even more valuable information in the near future.

From these recent studies it seems fair to conclude that cases of so-called "primary atypical pneumonia" are probably of varied etiology. It seems possible, however, that a single agent may be the cause of many or even most of the cases in a given outbreak, or in a single locality. In any event, the isolation of the causative agent is at best a tedious and painstaking procedure that must be carried out under the most exacting and controlled conditions.

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SELECTION OF OFFICER CANDIDATES

AN interesting and provocative study describing a method designed to select those men who possess the fundamental qualities that warrant their training as officers in the armed forces has been recently published by the Department of Hygiene of Harvard University.* The method combines three elements: an eight-minute test of physical fitness, a ten-minute interview to evaluate the man's total personality and, finally, a brief inspection of the body build to determine the characteristics of masculinity that "have been found to be related to physical fitness and officer fitness."

The authors have found that there is a high degree of accord between the results of their comparatively short examinations and the ratings given independently to the same candidates by commissioned officers of the Army or Navy based on a time-consuming study of all available data. There was, further, a remarkably close relation between the level of physical fitness and the evaluation made by the short personality interview. This, in turn, bore a close correlation to the body build. The implication seems to be that the expressions "athlete" and "officer" are to some degree synonymous, but the authors are careful to point out that "the physical fitness test should not be used alone for selection of officers with disregard of characteristics of personality that fit them for combat leadership." In this connection, it should be stated that the study is concerned chiefly with "officer material primarily for field and combat duties," although this distinction is not specifically indicated in the title of the monograph.

In general, the authors conclude that the best officer material is found among men with great physical stamina, as determined by the "step test," those having certain characteristics—such as alertness, steadiness, strength of character and sense of responsibility—that fit them for combat duty, and men with a high "masculine component," as determined by objective examination.

Any of the three parts of the examination is likely to be criticized by those especially interested in that particular aspect of the problem, and no doubt with further experience the criteria may be altered to a greater or less degree. In the meantime, much credit is due the authors for having come forth with a definite and, to some extent, definitive method for choosing those men of the armed forces who are most likely to be competent and responsible combat officers, surely a timely and valuable contribution.

*Woodruff W L, Remba L and Selzer C C *Selection of Officer Candidates* 46 pp Cambridge Harvard University Press 1945

MEDICAL EPONYM

WALDEYER'S RING

This was described by Professor H. Wilhelm G. Waldeyer (1836-1921), of Berlin, at the meeting of the Berlin Society for Internal Medicine on May 5, 1884, in a paper entitled "Ueber den lymphatischen Apparat des Pharynx [The Lymphatic Apparatus of the Pharynx]." This was reported in abstract in the *Deutsche medicinische Wochenschrift* (10: 313, 1884). A portion of the translation follows:

Since the discovery of the pharyngeal tonsil by Lacachie, the tubal tonsil by J. von Gerlach, and the establishment of the fact that the follicles of the tongue together represent a superficially spread-out tonsillar structure (the lingual tonsil), it is now evident that a ring of lymphatic tissue surrounds the whole region of the throat and upper pharynx, the course of which may be traced as follows: beginning with the pharyngeal tonsil, it extends to the region around the orifice of the eustachian tube (the tubal tonsil), thence to the faucial tonsil and down along the margin of the glossopalatine arch to the lingual tonsil, whence it crosses to the opposite side and follows a similar path back to the pharyngeal tonsil.

The tonsils simply represent marked accumulations of lymphatic tissue, which is nowhere absent in the above-mentioned region, being demonstrable even in all the intertonsillar spaces. The investigations of the speaker show that the lymphatic tissue also extends deeply into the nares as the center of the middle and lower turbinates and downward onto the posterior wall of the pharynx. This ring of adenoid tissue may be termed "tonsillar ring" or the "lymphatic ring of the throat."

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OBSTETRIC CASE HISTORY: PREGNANCY
COMPLICATED BY FIBROID — OPERATION

A thirty-three-year-old primipara was first seen when approximately two months pregnant. Her past history was essentially unimportant. She had had no contagious diseases or operations. Physical examination showed a normal and well-developed woman, weighing 120 pounds. The blood pressure was 122 systolic, 60 diastolic. External pelvimetry gave the following measurements: 28, 23 and 21 cm. On vaginal examination the cervix was posterior, and the fundus anterior; the latter was enlarged, and consistent with a pregnancy of eight weeks. Nothing abnormal was found about the uterus by palpation. A blood Wassermann reaction was negative, and urinalyses were normal.

Pregnancy was normal and uneventful until the eighteenth week, when discomfort and pain on the left side of the abdomen were sufficient to awaken the patient from a sound sleep. There was no nausea. The bowels had been regular. When seen, palpation revealed a tumor mass in the left flank, and the uterus seemed irritable. There was no fever. The patient was immediately transported to the hospital and given 10 mg. of Proluton. Her temperature during the first night in the hospital reached 100°F. It was 99.2°F. the next morning, and 99.8 at noon. The white-cell count was 23,000. The mass on the left was tender and seemed quite discrete.

The diagnosis lay between a strangulated fibroid and an ovarian cyst with a twisted pedicle. Consultation was held and operation advised. A flat plate of the abdomen was taken, but was inconclusive. At operation a tumor the size and shape of a medium-sized potato was found arising from the fundus on the left. It apparently was a fibroid and arose from a rather broad pedicle. This was excised, and the base tied with No. 1 chromic catgut. A smaller fibroid, about the size of a plum, on a pedicle was found anteriorly on the left. This was removed in a similar manner. A much smaller one, low down on the right, was also excised. There was practically no bleeding.

The pathological report was as follows: leiomyoma; active acute necrosis with polymorphonuclear infiltration.

Postoperative convalescence was complicated by a temperature of 99.4°F. and a pulse of about 100 for three days. There was little distention, and practically no nausea or vomiting. Subsequently, the temperature remained normal. The stitches were taken out on the tenth day, when the wound was well healed. The patient was discharged on the eighteenth day. Five milligrams of Proluton was given daily during the hospital stay.

The course of pregnancy was normal. Labor started at term. Cesarean was performed because of premature separation of the placenta. The baby weighed 7 pounds, 11 ounces. Convalescence was complicated by a febrile reaction that began on the third day, lasted forty-eight hours and reached a peak of 102°F., with a pulse of 90; this was due to a saprophytic infection. The patient was discharged on the eighteenth day.

Comment. Fibroids occurring during pregnancy are not uncommon and usually are not serious complications. If a fibroid is in the lower segment and is so big that it occludes the pelvic inlet, pelvic delivery is impossible and cesarean section is indicated. Strangulated fibroids, such as the one in this case, are practically always subperi-

toneal and arise from a moderately broad base. Fibroids in the muscle of the uterus rarely become strangulated during pregnancy. Many of them become tender and are painful, but the majority quiet down and do not require surgery.

Operation in this case was advised for two reasons. In the first place, the diagnosis was uncertain. One consultant thought that the tumor was an ovarian cyst and another that it was a fibroid. In either case, the elevated temperature and white-cell count and the tenderness of the tumor indicated surgery. The separation of the placenta, which necessitated cesarean section, occurred during labor when the cervix was not ready for vaginal delivery. When the uterus was opened, more placenta was found to be separated than was thought probable. The uterus was filled with meconium. The membranes were necrotic, and the musculature at the placental site was bluish and rather spongy. There is no reason to infer that the separation of the placenta in any way resulted from the myomectomy.

WAR ACTIVITIES

CIVILIAN DEFENSE

EMERGENCY MEDICAL SERVICE IN INDUSTRIAL PLANTS

The following directive was recently released by the Medical Division of the Office of Civilian Defense, Washington, D C.

Every plant medical department should prepare a disaster-operations plan to provide adequate medical service in case of a plant catastrophe involving large numbers of casualties. This is the advice presented in a new bulletin, *Emergency Medical Service for Industrial Plants*, issued by the Medical Division of the Office of Civilian Defense.

The War and Navy departments have urged that plants for which they are responsible plan to use the facilities and services of the Emergency Medical Service organized by civilian-defense authorities. The Medical Division has in turn urged that local chiefs of Emergency Medical Service assist plant medical departments by placing the community medical facilities at their disposal in the event of a major emergency, regardless of its cause.

Pointing out that plant medical departments are not ordinarily staffed or equipped to provide medical service for the large number of casualties that may occur in a major disaster, the bulletin outlines arrangements that should be made to assure adequate medical care at such times.

The disaster-operations plan should provide for necessary first aid care at the site of the incident, for adequate ambulance service and for hospitalization of the seriously injured. The bulletin advises:

Provision must first be made for casualty stations. Several sites should be selected, in order that alternative locations may be used in case those of first choice are destroyed or rendered unserviceable. An additional site outside the plant should be selected for use in the event of extensive damage to the plant, such as might occur in a bombing or explosion.

The importance of identification and records is especially emphasized in the bulletin.

In any disaster, confusion will be inevitable, it is pointed out. It will be difficult, without adequate records, to identify the seriously injured and the dead and to determine the number and names of the missing. The uninjured as well as the injured should be accounted for. A record should be made of every person who leaves the plant. The record should indicate the places to which the injured have been taken.

In a consideration of transportation, the bulletin recommends that arrangements be made with the local chief of Emergency Medical Service to ensure that ambulances under his direction will be made available to the plant should a disaster involve the entire community. Similarly, any ambulance facilities owned by the plant should be made available to the local chief if they are not required at the plant.

Present plans for the hospitalization of industrial accident victims are likely to be grossly inadequate in the event of a major plant catastrophe, the bulletin declares. Large numbers of patients should not be sent to one hospital if other hospitals are available. To provide quick and efficient service to injured persons, casualties should be distributed among various hospitals. Arrangements must be made with the local chief of Emergency Medical Service for the admission of casualties to community hospitals, all of which will be under his supervision during a major emergency.

A prerequisite to the entire plan of mutual aid between a plant and a community is a definite understanding that members of the Emergency Medical Service will be admitted promptly to a plant in an emergency. To assist plant managers to carry out their duty in keeping unauthorized persons out of war production plants and to facilitate the admission of physicians when they are needed, the service commands of the Army are conducting investigations of the key personnel of the Emergency Medical Service. Personnel investigated and approved by a service command will receive identification cards from the Office of Civilian Defense.

The bulletin sketches the organization and operation of protective services in a community, and the over-all protective services recommended for industrial plants. It also outlines the program of federal compensation for injuries to civilian defense workers and explains how this plan applies to industrial workers. A bibliography of pertinent material is included.

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

The second meeting of the New England Pathological Society was held on January 21, 1943, at the Peter Bent Brigham Hospital.

The first paper of the evening, *Simple Tissue Extracts*, was given by Dr. Sidney Farber. Acetylcholine may be extracted from normal tissues by treating minced tissue initially with ethyl alcohol, sulfuric acid, or trichloroacetic acid and subsequently filtering, shaking with ether and concentrating at low pressure. Although extracts prepared in this manner contain large quantities of other pharmacologically active substances, the presence and amount of acetylcholine may be determined by suitable biologic tests, which permit the exclusion of sub-

stances such as potassium, histamine and adenosine compounds. Since acetylcholine cannot be diffusible freely in tissues in amounts obtained from extracts because of the rapid destruction by choline esterase, it has been suggested that the substance is stored in some special structure that prevents it from diffusing freely through the tissue. Some observations bearing on this point were made in the course of experiments conducted in collaboration with Dr. Ernest K. Landsteiner and Dr. Alfred Pope. It was found that, when small pieces of certain normal organs of the freshly killed rat, guinea pig, rabbit or cat were immersed for a few minutes to a few hours in a bath of Ringer's solution containing physostigmine, there could be demonstrated in the Ringer's solution a substance that had the pharmacologic properties of acetylcholine. All extracts were tested on two preparations of the dorsal muscle of the leech, one of which was eserized. Verification of the nature of the substance was given by its depressor action, after intravenous injection, on the blood pressure of the cat and the rabbit, with intensification of the effect after physostigmine and disappearance after atropine. The most active extracts were obtained from the intestinal tract. Positive results also were obtained from the brain, the lung, the heart, the bladder and sometimes the kidney. Skeletal muscle, testes, spleen and liver gave negative results. The effects of the pH of the Ringer's solution, the time and the temperature and species differences were studied.

The ready liberation into saline solutions of a substance presumably acetylcholine from decomposing tissue under the conditions employed made it of interest to ascertain whether acetylcholine might be liberated from areas of tissue destruction in the living body. Accordingly, in a series of experiments conducted with the assistance of John Carabitses, intestinal obstruction was produced in rabbits under Nembutal anesthesia by ligation of a large part of the bowel. In the clear fluid that collected in the peritoneal cavity within four to eight hours after the onset of the obstruction a substance was demonstrated that appeared to have the properties of acetylcholine. Greater amounts were observed in the fluid that had collected within the obstructed portion of the bowel and in saline extracts of the necrotic bowel itself. No conclusions were drawn concerning the significance of this finding. Acetylcholine should be added to the group of substances that may be found in extracts of the intestinal tract. This includes potassium, adenosine compounds, histamine and Gaddum's substance P.

The second paper was given by Dr. Charles E. Dunlap, the subject being "Transplantable Osteogenic Sarcomas Induced in Rats by Feeding Radium." Osteogenic sarcomas appeared in the vertebrae and pelvic bones in 9 of 13 male Wistar rats after feeding each animal 100 microgm. of radium. Within ten days after feeding, the animals had excreted 95 per cent of the radium. The average amount retained at the end of one year was only 2 microgm. The induction time from the first radium feeding to the discovery of the tumors was 253 to 426 days, averaging 365 days. Two of the nine primary tumors metastasized, one to the pelvic lymph nodes and one to the spleen. Three of the tumors were successfully transplanted to other rats, and one has been maintained through seven serial generations. In addition to the osteogenic sarcomas, all the rats showed widespread necrosis of bone, and atypical new-bone formation was found in all but one. The bone marrow was hypoplastic and showed generalized immaturity and abnormal deposits of hemosiderin. Marked hemosiderosis was present in the spleens, together with extramedullary hematopoiesis. Thus, the pathologic changes consequent to ra-

dium poisoning in human beings were reproduced in rats with a fair degree of fidelity and a readily transplantable osteogenic sarcoma of rats was obtained.

In the discussion of the paper the question was raised by Dr. Earle Clark whether the tumor arose from the periosteum or the periphery of the bone. Dr. Dunlap replied that there was a definite question in his mind whether some of them did not arise from the subperiosteal tissue. The question whether similar changes were produced by injection of radioactive phosphorus having a half-life of fourteen and a half days was raised. Dr. Shields Warren stated that although selective deposition in bone of the phosphorus was somewhat comparable, there was not the same effect on the bone structure or the bone marrow. He also pointed out that the radioactivity of phosphorus was due to the beta radiation and that in Dr. Dunlap's cases it was the alpha ray which was responsible for the marrow changes and tumor formation.

The third paper of the evening, "The Effect of Crystallized Bovine Albumin on the Tissues of Normal Animals," was given by Drs. Orville Bailey and Clinton van Hawn. The methods for the fractionation of plasma protein recently developed in the Department of Physical Chemistry of the Harvard Medical School have made available the proteins of blood plasma in states of great purity and in far larger amounts than could have been obtained by previous methods. The albumin of human plasma has already been used in the clinic. To provide larger amounts of material for use in shock, Cohn and Hughes have prepared crystallized albumin from bovine plasma. Before using this material as a therapeutic agent in man, it seemed advisable to determine its effects on animals. Normal rabbits were injected intravenously with crystallized bovine albumin in 25 per cent solution in doses of 1 gm. per kilogram of body weight. Animals were sacrificed at various intervals after one, two, seven and twelve injections. No change in state of nutrition or behavior was noted in the rabbits. Slight enlargement of the spleen was the only change noted grossly. Histologically there was an increase in the amount of phagocytosis of leukocytes and red blood cells in the pulp and sinusoids of the spleen. This was regarded as an accentuation of a process occurring in the spleen of normal rabbits. Similar sequences of phagocytosis of blood cells were found in the Kupffer cells of the liver, in lymph nodes and in the bone marrow; in these organs, however, the process took place only to a slight extent. In the kidneys there were swelling and dispersion of the epithelium in the ascending limb of Henle's loop and in the distal convoluted tubules. These changes were regarded as an indication that some of the albumin was filtered through the glomerulus and entered the tubular epithelial cells more rapidly than it was reabsorbed in the circulating blood. The histologic changes in all organs were reversible, the organs eventually returning to a normal state, even after twelve injections.

Mice were injected intraperitoneally with a 25 per cent solution of crystallized bovine serum albumin. A single injection of 1 cc. produced no tissue changes. Thirty similar injections led to slight and rapidly reversible changes in the spleen and kidneys. When 2-cc. doses were injected daily, marked but reversible alterations in the kidneys appeared after ten or more injections. These amounts of albumin were far in excess per kilogram of body weight of the quantities used clinically; however, the studies indicated that the first organ to show evidence of severe injury as the dosage of crystallized bovine serum albumin was increased to excessively high levels was the kidney. No "storage disease" or amyloid

deposition was found in either rabbits or mice under the experimental conditions used.

Because of species differences, it is hazardous to assume that the tissue reactions to crystallized bovine albumin in man are the same as those of the rabbit or the mouse. However, the tissue reactions induced in either experimental animal by injections comparable per kilogram of body weight to those contemplated in man would not contraindicate the use of the material were they to occur in human patients.

In the discussion that followed the question was raised whether injections of the glomeruli with the cold solutions would give more albuminuria, as has been reported by Dock. It was stated that this phenomenon was not observed because only intact animals were used in the experiments.

The fourth paper of the evening, "The Mechanism of Enhanced Diabetes with Inflammation," was given by Dr. Valy Menkin. The enhanced course of the diuretic condition with superimposed inflammation or infection is clinically well known. An inquiry into the basic mechanism concerned in explaining this intensified condition was undertaken by Dr. Menkin. The observations and conclusions drawn are summarized as follows:

The data have been obtained from depancreatized dogs. This form of experimental diabetes has many obvious points of similarity to the human disease. Nevertheless, it is to be recalled that there are also several notable differences. Depancreatized dogs with superimposed inflammation in the pleural cavity, induced by previous injection of turpentine tend (with few exceptions) to develop a marked rise in their already existing hyperglycemia. Pleural inflammation per se in nondiabetic animals fails to alter appreciably, or at least in a sustained way, the blood sugar. In depancreatized dogs the presence of a concomitant inflammation has been followed by an average increase of 216 mg in the concentration of blood sugar. In order to determine the responsible mechanism involved, two considerations have to be kept in mind. In the first place, glucose can be derived to a certain extent from proteins as a result of deamination. Thus, gluconeogenesis from proteins is a well known phenomenon. It is also important to recall that insulin tends first to repress glucose formation from such noncarbohydrate precursors of glucose. In the second place, proteolysis is a cardinal biochemical feature of inflammation. It is conceivable that the mechanism of enhanced diabetes with superimposed inflammation may be referable to an augmented degree of proteolysis at the site of inflammation with a corresponding increase in glucose formation from products of protein breakdown. The abundant glucose formed at the site of injury in turn diffuses into the circulating blood, thus giving rise to the excessive hyperglycemia. At the same time the enhanced local proteolysis reasonably explains the tendency for the appearance of marked cell damage or increased severity of the inflammatory reaction.

This hypothesis has been fully supported by experimental observations. In brief, the exudate sugar, lactic acid, urea, nonprotein nitrogen, and amino-acid nitrogen have all been found to be markedly increased in diabetic dogs as compared with the levels in nondiabetic preparations. The exudate sugar has increased in the diabetic animals on an average of 47 per cent, the lactic acid, 52 per cent, the urea, 126 per cent, the nonprotein nitrogen 89 per cent and the amino-acid nitrogen 74 per cent. At the same time the total protein of exudate in diabetic dogs is on the average 13 per cent lower than that encountered in nondiabetic animals. These facts therefore substantiate the marked increase in proteolysis in the

exudates of diuretic animals and the corresponding high glucose content at the sites of inflammation. It is of great significance to note that insulin administration not only lowers markedly the glucose concentration of exudate but likewise represses the increased local proteolysis. This fact strongly supports the view that the excess glucose formation at the site of inflammation seems to be derived primarily from products of protein breakdown. The products as well as the formed glucose are highly diffusible and are consequently not fixed at the site of inflammation. They penetrate readily into the circulation. The result is not merely an exaggerated hyperglycemia; there is also a reflection of the elevated products of nitrogenous metabolism from the exudate into the blood stream. Furthermore an examination of the leukocytes at the site of inflammation indicates that with the greater degree of proteolysis and the elevated lactic acid production found in diuretic exudates these cells show striking signs of injury and degeneration. In this way the combination of lowered pH and enhanced local proteolysis offers an explanation for the increased cell damage of inflammation in diabetic animals.

More recent studies have indicated that abundant glucose at the site of inflammation originates from the injured cells and that the sugar then gradually diffuses into the circulation rather than the reverse order of sequence. Careful comparisons of the sugar concentrations in the exudate and in the blood at various stages of the inflammatory reaction indicate that at first the exudate sugar is at a considerably higher level than the blood sugar. The latter at first shows no appreciable increase over the level found following pancreatectomy. It is only after the reaction in the pleural cavity has progressed for about one day or slightly less that sufficient glucose has diffused from the site of inflammation into the blood stream to reveal a manifest rise in the hyperglycemia. Thus the establishment of a conspicuous gradient in the glucose concentration between exudate and blood supports the view of a gluconeogenic process at the site of inflammation in the diabetic animal. A similar gradient, although not so pronounced, is found in the case of urea. The evident quantitative difference between the behavior of these two substances seems referable to the difference in the diffusion coefficient of glucose and urea. Observations in nondiabetic animals indicate a transitory gradient in the glucose concentration found in exudate and blood. The provisional nature of the gradient is referable to the marked glycolytic reaction at the site of inflammation, which in the nondiabetic animal quickly overshadows the process of local gluconeogenesis. In this way the essential difference between the diabetic and the nondiabetic animal becomes virtually a quantitative one. The overproduction of glucose at the site of inflammation in depancreatized animals fails to be appreciably affected by glycolysis. The latter reaction, however, in the exudate of nondiabetic dogs soon transcends gluconeogenesis. Nevertheless these observations point to a basic principle, namely, that inflammation injured cells per se become potential foci of glucose formation. So far as this particular function is concerned, an area of inflammation therefore assumes to some extent the capacity of the normal liver. This becomes merely exaggerated in an inflamed area of a diabetic animal.

In conclusion, the basic mechanism of diabetes enhanced by superimposed inflammation seems primarily referable to an increased proteolysis at the site of injury. This is followed by excessive glucose formation from nitrogenous sources, the glucose, in turn, diffuses gradually into the circulation giving rise to a marked hyperglycemia.

In the discussion of the paper Dr. Sidney Farber raised the point whether loss of nitrogen and fat in the stools would produce fatty changes of the lipocaic-deficient type. Dr. Menkin stated that no changes were evidenced when raw pancreas and choline were added to the diet.

BOOK REVIEWS

Aftereffects of Brain Injuries in War: Their evaluation and treatment, and the application of psychologic methods in the clinic. By Kurt Goldstein, M.D. With a foreword by D. Denny-Brown, M.D. 8°, cloth, 244 pp., with 46 illustrations and 2 plates. New York: Grune and Stratton, 1942. \$4.00.

The author for many years worked in a special hospital in Germany with patients who had suffered structural injury to their brain during World War I. There he carried on extensive psychologic studies, which were reported from time to time in the German literature. Since coming to this country these studies have been translated into English and now are put together in an attractive volume of outstanding worth. The author's knowledge of the psychology of patients with brain injury is extensive and he gives in detail the findings incidental to his long experience. The book is not for the practitioner but for the specialist in injuries to the nervous system. It will show him the work that has been done in this complicated field and will point out how little we really know about psychotherapy based on structural damage.

The latter part of the book takes up the treatment of patients with severe brain damage, particularly the training of those with speech defects, one of the most marked disabilities that can follow injury. The author is careful to set down his methods and tells of the results that he has obtained. In general he is frank and states that few patients can be cured by individual effort, since it requires the teamwork of a specialized hospital in which physicians, nurses, orderlies and occupational therapists work together to improve the patient's condition.

The last point is worth reiteration, although it has been widely recognized since World War I. One of the plans of the late Harvey Cushing was to develop an institution along these lines, but the plan was thwarted by the difficulty in having patients centralized in such a large country as the United States. It is hoped, however, that such a plan may come into effect after the present crisis, since, thanks to increased facilities for the transportation of patients, the country is no longer so large as it was in 1920. Patients are now easily moved by aeroplane, and one can visualize a great hospital in such a central place as Chicago, with patients coming from all parts of the country.

Occupational Tumors and Allied Diseases. By W. C. Hueper, M.D. 4°, cloth, 896 pp. Springfield, Illinois: Charles C Thomas, 1942. \$8.00.

This monograph provides an extensive and well-organized source of information concerning the various aspects of neoplastic lesions and allied diseases of probable occupational origin. After a discussion of the history, concepts and significance of these particular tumors the material is arranged by sections, corresponding to the systems of the body that are involved. Stress is laid on lesions of the skin, respiratory, alimentary and urinary systems, blood-forming organs and mesenchymal tissues. There is detailed information concerning the nature and source of the exciting and accessory etiologic agents. The histologic features, symptoms, diagnosis and treatment of the tumors in question are discussed comprehensively. The

book closes with chapters on the relation of occupational neoplasms to the theories of carcinogenesis and on the medicolegal and public-health aspects of the problem. There is an extensive bibliography; the total number of references is well over 3500, and it is obvious that little of importance has been omitted. This in itself greatly enhances the value of the book.

Throughout, the author attempts to sift the available data and theoretical concepts of these tumors and to analyze and integrate the material to provide a coherent picture of each specific lesion. Aside from a few contradictions, it may be said that he has admirably succeeded in a most difficult task.

Frequently, the sentences are excessively long and complicated, which distracts one from the picture the author wishes to create. Furthermore, a summary of the pertinent material at the end of each chapter would be extremely helpful. The subject index, although adequate, would greatly improve the value of the book if it were more complete.

The incidence of occupational tumors has increased considerably as a result of the rapid development of industry in the last few decades. Consequently, a knowledge of these diseases is of extreme importance, and hence this monograph fulfills a definite need. Because of its wide scope, it can be recommended for all physicians and others who have to deal with industrial disease. The author and the publisher are to be congratulated on their painstaking work in the preparation of this volume.

Roentgen Treatment of Diseases of the Nervous System. By Cornelius G. Dyke, M.D., and Leo M. Davidoff, M.D. 8°, cloth, 198 pp., with 12 engravings, 7 charts and 16 graphs. Philadelphia: Lea and Febiger, 1942. \$3.25.

This is an important book on a subject little understood. Only in the last decade or two have there been a sufficient number of cases of diseases of the nervous system under observation in one clinic, treated by adequate doses of roentgen rays and followed for a number of years for an evaluation of this type of therapy to be made. The senior author, Dr. Dyke, is radiologist to one of the largest neurological centers in this country, and the junior author, Dr. Davidoff, has long been recognized as an outstanding neurosurgeon, trained in the clinic of the late Harvey Cushing.

Over half the book deals with brain tumors. Each type of tumor is considered separately. The data on a number of treated cases are followed by one or two selected case histories and a general discussion of the effects of roentgen rays on the type of tumor under consideration. Each section is accompanied by graphs illustrating the amount of treatment, the time when it was given and the reaction of the patient. The amounts are given in totals, not in individual doses. Thus, by knowing the type of tumor, rapid information can be found in this book in regard to the use of roentgen rays as a form of treatment.

Another section of the volume deals with the treatment of spinal-cord tumors, infectious and inflammatory diseases, and miscellaneous conditions. A preliminary section of the book gives the technic of roentgen-ray treatment as developed in various centers in this country.

The book is thus a complete, up-to-date treatise on the subject, with a good working bibliography and an excellent index. To all neurosurgeons, neurologists and radiologists, this book is highly recommended.

(Notices on page viii)

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COMPOUND FRACTURES OF THE SKULL*

The Results of Surgical Therapy in Two Hundred and Eighteen Cases

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BOSTON

WITH the advent of the sulfonamide group of drugs there has been a tendency among members of the medical profession to discard the results of the studies that have been made in previous years along other lines, and to substitute chemotherapy in their place. Since the entrance of the United States into the war, when the need for dealing with battle and air raid casualties arose, this tendency has been particularly apparent in the field of surgery. This, together with the ill considered lay magazine and newspaper publicity that followed the first reports of the neurosurgical and other casualties at Pearl Harbor, calls for a critical analysis of what properly conceived surgery is able to accomplish without the aid of chemotherapy. The object of this analysis is to discover whether chemotherapy can justifiably be expected to be of assistance in this problem, and whether the indiscriminate use of chemotherapy may do harm even beyond the point of leading to the neglect of fundamental surgical principles that have successfully stood the test of time. The need for this knowledge is especially acute in traumatic craniocerebral surgery, and in particular in compound fractures of the skull. Of necessity, the great majority of these cases will have to be cared for by general surgeons who are not experienced in this field. They appreciate their lack of experience and the deficiencies that go with that lack more keenly than anyone else, and are only too eager to profit from the experiences and mistakes of others.

The data presented herewith, together with a review of certain pertinent articles in the English and Canadian literature, are the result of eleven years' experience with patients suffering from injuries to the central nervous system. They are presented chiefly to emphasize that although

chemotherapy with the sulfonamides is indispensable, it cannot and should never be used as a substitute for properly conceived surgery in the treatment of compound fractures of the skull.

Up to January 1, 1942, 218 cases of all types of compound fracture of the skull have passed through my hands. These were divided as follows: 29 involved one or more paranasal air sinuses but had no cerebrospinal rhinorrhea, 12 patients had cerebrospinal rhinorrhea, either with or without involvement of a paranasal air sinus, 16 had bullet wounds, 6 had perforated wounds, 2 had a complicating avulsion of the scalp, and 153 had simple compound fractures.

In addition to the compound fractures of the skull, 23 patients had major injuries in other parts of the body. Twenty of these had fractures of other bones as follows: lower extremity, 9 cases (pelvis, 2, femur, 2—one compounded and accompanied by a fractured ilium, both bones of the lower leg, 3—one comminuted into the knee joint, tibia, 1, and fibula, 1), upper extremity, 9 (clavicle, 2, humerus, 1, both bones of the forearm, 2—one accompanied by a fracture of the olecranon of the other arm, radius, 1, and Colles's fracture, 3—one comminuted into the wrist joint), spine, 1, and facial bones, 1. Three patients had multiple injuries, all accompanied by a ruptured lung and 1 by edema of the glottis in addition.

Sixteen patients had other severe associated cranial or intracranial damage. Three had multiple compound fractures of the skull, one accompanied by exsanguination, and 2 had crushed skulls, one in addition to other injuries. Three patients had ruptured cranial venous sinuses, one with an extradural hematoma. Five had subdural hematomas, one with an extradural clot. There were 3 cases of severe ocular injury. In two of these one optic nerve was completely severed, and in one the other nerve was also par-

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tially severed; the third patient had a hemorrhage into the anterior chamber of one eye. Other complicating conditions were: syphilis, 4 cases, acute alcoholism, 3; severe heart disease, 2; toxic dehydration, 2; and miscellaneous conditions, 11—1 case each of intracranial tumor, decerebration, epilepsy, carotid-artery and jugular-bulb fistula, osteomyelitis of skull, psychosis, puncture wound of the right knee, gas-bacillus infection of a wound of

refused operation. In 3 others it is not clear from the record what the reason was. Only in the remaining 7 (12 per cent) did the surgeon have a legitimate opportunity to exercise his judgment and elect not to operate. In two of these 7, the compounded fracture involved the anterior wall of one frontal sinus only, in another two there was a complicating extensive avulsion of the scalp, and in one the fracture was compounded directly over

TABLE 1. Age Incidence.

AGE	SIMPLE	TYPE OF COMPOUND FRACTURE					TOTAL
		INVOLVING FRONTAL SINUS, WITHOUT RHINORRHEA	INVOLVING FRONTAL SINUS, WITH RHINORRHEA	WITH AVULSION OF SCALP	BULLET WOUNDS	INFILTRATING WOUNDS	
57							
Under 10	47	1	4		1	2	55
10-19	20	1	1		3	1	26
20-29	21	6	2	1	4	1	35
30-39	17	9			1		27
40-49	12	8	2	1	3		26
50-59	19	1			1	2	23
60-69	7	2	1				10
70 or over	4	1	1		1		7
Not known	6		1		2		9
Totals	153	29	12	2	16	6	218

the leg, pyelitis, pregnancy and inoperable carcinoma of the rectum.

All age groups were represented, the youngest patient being three months old and the oldest eighty-one years (Table 1). The largest single group (55 cases) was made up of children under ten years of age. Among them were 26 that were five years old or younger. Seven patients were over seventy.

Sixty of these 218 patients died, a mortality of 27.6 per cent (Table 2). There were one hundred and fifty-nine operations—an operability rate of 73 per cent. No patient was operated on more than once. Twenty-five of these 159 patients died—an operative mortality of 15.7 per cent. In contrast to this, there were 59 patients who were not operated on. Thirty-five of this group died—a mortality of 59.3 per cent. A study of the reasons that lead to a decision not to operate indicates that not only these injuries but those in all the patients were at least as severe as, and probably severer than, any average similar group. Operation was decided against because of surgical shock in 27 cases, poor general condition in 7, other complicating major injuries or infection in 5, and because the patient was admitted too late in 5. Thus, 44 (75 per cent) of the 59 patients were not operated on because of adequate reasons that were beyond the control of the surgeon. In addition, 4 patients were not operated on because the diagnosis was missed, and 1 because the patient

the superior sagittal sinus. In a patient with cerebrospinal rhinorrhea, the fistula closed spontaneously in twenty-four hours, and in another, chemotherapy was substituted for surgery.

It is obvious that in this series, at least, the presence of surgical shock and analogous allied conditions constituted a major factor in reaching a decision concerning operability. By the same token, these same conditions played a most important part in determining the length of time that had of necessity to be allowed to elapse after the infliction of the injury and before operation could be undertaken without prohibitive risk.

Four principles have governed the therapy of compound fractures of the skull in my clinic. The first is that all compound fractures of the skull must be completely débrided within forty-eight hours of the infliction of the injury, or else not operated on until the wound has been completely healed for six to eight months, depending on the type and degree of infection. The second principle is that no patient shall be operated on until he is out of surgical shock and until his general condition warrants it. The third is that after the diagnosis has been made by palpation through the wound by the surgeon's sterilized finger, the first dressing shall be one that can be applied with an absolute minimum of handling of the wound. The fourth is that the débridement shall be complete unless there is a communication with the nose or involvement of the supraorbital ridge, shall be done

in such a way as to avoid spreading the bacterial contamination throughout the wound or producing tissue necrosis through tight sutures, and shall include the removal of all large foreign bodies. No wound that has been properly and therefore com-

juries are prone to operate early. It is axiomatic, of course, that the earlier one can débride such a wound, the better the chances of preventing the contamination in the wound from becoming an infection. This axiom holds good, however, only

TABLE 2 *Mortality and Sepsis Rates*

TYPE OF COMPOUND FRACTURE	ALL CASES				UNOPERATED CASES			
	TOTAL	DEATHS	24 HR. DEATHS	MORTALITY %	TOTAL	DEATHS	24 HR. DEATHS	MORTALITY %
Simple	153	40	23	26.1	41	28	23	68.6
Involving paranasal sinuses, without rhinorrhea	27	11	0	38.0	2	0	0	0
Involving paranasal sinuses with rhinorrhea	12	2	0	16.6	3	1	0	33.3
Bullet wounds	16	7	6	43.7	9	6	6	66.6
Perforating wounds	6	0	0	0	2	0	0	0
Avulsion of the scalp	2	0	0	0	2	0	0	0
Totals	218	60	29	27.6	59	35	29	59.3

TYPE OF COMPOUND FRACTURE	ALL OPERATED CASES					ADJUSTED OPERATED CASES*				
	TOTAL	DEATHS	MORTALITY %	SEPTIC CASES	PER CENT AGE OF SEPSIS	TOTAL	DEATHS	MORTALITY %	SEPTIC CASES	PER CENT AGE OF SEPSIS
Simple	112	12	10.7	31	27.6	91	4	4.4	6	6.6
Involving paranasal sinuses, without rhinorrhea	27	11	27.6	6	27.2	21	6	28.5	2	9.5
Involving paranasal sinuses, with rhinorrhea	9	1	11.1	0	0	9	1	11.1	1	11.1
Bullet wounds	7	1	14.2	1	14.2	6	1	16.6	1	16.6
Perforating wounds	4	0	0	1	25.0	3	0	0	0	0
Avulsion of the scalp	0	0	0	0	0	0	0	0	0	0
Totals	159	25	15.7	39	24.5	130	12	9.2	10	7.6

*Figures corrected for technical errors

pletely débrided has been drained. In all undrained wounds, unless the wound heals by first intention and without evidence of infection of the scalp, bone, meninges or brain, it is considered to be a septic one and the result to be unsatisfactory. Drained wounds are not expected to heal by first intention or necessarily to be free of meningeal infection. Deaths caused by postoperative sepsis in any form are not considered justifiable, and an attempt is made in every such case, as well as in every case of postoperative sepsis following a drained or undrained wound, to determine the proximate cause of the sepsis and death.

The first and second principles noted above have to do with determining the optimum time of operation. There can be no doubt that such a major procedure as débridement of a compound fracture of the skull should not be attempted until the patient is out of surgical shock and until his general condition is such as to do away with any risk that prohibits operation. It is apparent that there is a wide variation in the severity of the compound fractures of the skull seen in different neurosurgical clinics, and that those surgeons who see a small percentage of severe in-

juries are prone to operate early. It is axiomatic, of course, that the earlier one can débride such a wound, the better the chances of preventing the contamination in the wound from becoming an infection. This axiom holds good, however, only if the increased risk of death without infection as the result of a relatively immediate operation is properly assessed against the increased risk of infection without death from a postponed operation. The crux of this problem lies in the speed with which a contaminated wound metamorphoses into an infected wound in the absence of any extraneous factor, such as manipulation or operation. In the absence of evidence to the contrary, and on the basis of experience collected previous to the present war in analogous lesions of the long bones, this time has commonly been set at six to eight hours. My experience has convinced me that this period is needlessly short from the point of view of the bacterial content of the wound of compound fractures of the skull, and dangerously short from the point of view of risk to the patient's life.

Work by Miles,¹ Spooner,² Hare and Willits,³ Smith⁴ and others, moreover, suggests strongly that from the bacteriologic aspect the incidence of infection, as opposed to contamination of compounded wounds of the long bones and extremities, is unexpectedly low during the first forty-eight hours after infliction, and that much more im-

portant factors in the control of wound infection in such cases are the immediate and as nearly as possible complete immobilization of the wound and the avoidance of cross infections from attendants, including physicians and nurses, other patients, dressings and bed linen. The importance of these sources of infection has also been emphasized by Trueta⁵ and Barnes.⁶ Cairns⁷ has stated in relation to craniocerebral injuries that patients

poned if necessary up to forty-eight hours after infliction of the wound without significantly increasing the risk of wound infection. On the other hand, because of the high rate of culturability (91 per cent), operations performed on these wounds after the first forty-eight hours following infliction have a prohibitive and unjustifiably high rate of infection. As stated above, if the wound is not manipulated, compound fractures of the skull

TABLE 3. *Organisms Recovered from Wounds of Compound Skull Fractures.*

ORGANISM	SIMPLE COMPOUND FRACTURES			COMPOUND FRACTURES INVOLVING PARANASAL SINUSES WITHOUT RHINORRHEA			COMPOUND FRACTURES INVOLVING PARANASAL SINUSES WITH RHINORRHEA			BULLET WOUNDS			PERFORATING WOUNDS			ALL FRACTURES		
	RECOV-ERED CASES	FA-TAL CASES	TO-TAL CASES	RECOV-ERED CASES	FA-TAL CASES	TO-TAL CASES	RECOV-ERED CASES	FA-TAL CASES	TO-TAL CASES	RECOV-ERED CASES	FA-TAL CASES	TO-TAL CASES	RECOV-ERED CASES	FA-TAL CASES	TO-TAL CASES	RECOV-ERED CASES	FA-TAL CASES	TO-TAL CASES
<i>Str. haemolyticus</i>	1		3	0	0	0	0	0	0	0	0	0	0	0	0	1	2	3
<i>Str. haemolyticus</i> and <i>Staph. aureus</i>	2	1	3	0	1	1	1	0	1	0	0	0	0	0	0	3	2	5
<i>Staph. aureus</i>	21	0	21	0	1	1	2	0	2	2	2	4	1	0	1	26	3	29
<i>Staph. albus</i>	7	0	7	0	0	0	0	0	0	0	0	0	0	0	0	7	0	7
<i>Meningococcus</i>	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
No growth	9	0	9	1	0	1	1	0	1	0	0	0	0	0	0	11	0	11
Totals	40	3	43	1	3	4	4	0	4	2	2	4	1	0	1	48	8	56

do better if operation is postponed until their general condition is satisfactory and they have been transported to a hospital where adequate facilities are at hand. This has also been the Continental experience, especially in regard to postponement pending the availability of proper equipment and personnel, as evidenced by Jentzer⁸ and Tönnis.⁹

I¹⁰ recently made a study of the bacteriology of compound fractures of the skull in 52 patients (Table 3). Although all such wounds were considered to be contaminated at the time of infliction, positive cultures of pathogenic bacteria were obtained from only 55 per cent of cases in the first twenty-four hours and from only 66 per cent in the first forty-eight hours after infliction. On the other hand, pathogenic bacteria were cultured from 91 per cent of the wounds swabbed later than forty-eight hours after infliction. I have been unable to find other similar bacteriologic studies of compound fractures of the skull. I am therefore convinced that, pending more complete evidence, although all compound fractures of the skull are probably contaminated at the time of infliction, the degree of contamination is so small that in the absence of manipulation of the wound, cultures can be grown from only half the wounds in the first twenty-four hours and from only two thirds of them in the first forty-eight hours. It seems only reasonable to conclude that in the presence of such a small increase in culturability, excision of the contaminating bacteria can be post-

should be operated on as soon as the patient's general condition permits major surgery to be performed with safety. Otherwise the débridement may be postponed up to forty-eight hours after infliction, but no longer without materially increasing the risk of changing contamination into infection of the wound and thus producing post-operative sepsis. It is during this postponement that chemotherapy by one of the sulfonamide compounds proves to be of great value. If administered promptly and in adequate dosage by mouth and sprinkled in and about the wound at the earliest possible moment without manipulation of the latter, its bacteriostatic power will further guarantee the patient against wound infection during any necessary waiting period previous to operation.

The third and fourth principles noted above are concerned with the avoidance of measures that spread the contaminating bacteria to hitherto uninvaded parts of the wound. They apply to the preoperative period as well as to the operation itself. Attention has been called to the fact that modern experience has demonstrated that immediate complete immobilization is the most important and essential guarantee against the spreading of infection in compound fractures and other wounds of the extremities. It has been shown that, aside from spreading by contact and the like, the lymphatics play the chief rôle in this dissemination.⁶ In bruising wounds it is certainly theoretic-

cally possible, and indeed probable, that owing to the local crushing effect the lymphatics and small veins at the circumference of the bruised area are at once closed mechanically and that they remain so for a variable number of hours. During this period, the contaminating bacteria are locally static unless these veins and lymphatics are opened up by manipulation, or until sufficient bacterial growth

and the larger the amount of irrigating fluid, the greater the cleansing effect. Where the walls and base of such a wound are solid and there is no communication with other cavities, all the ingoing fluid will return to the outside and the cleansing will be maximum and unaccompanied by any untoward side effects. This is the situation that exists in compound fractures of the long bones.

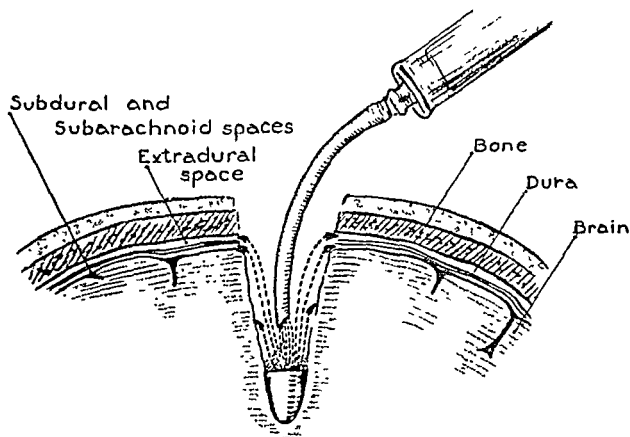


FIGURE 1. *Diagrammatic Representation of the Irrigation of a Bullet Tract in the Brain.*

has taken place to cause implantation of daughter cultures outside the limits of the contusion.

Mechanical transfer of bacteria to other hitherto uncontaminated areas can serve as another and important means of spreading infection. Such procedures as instrumentation and retraction of the tissues and irrigation of the wound act in this way. So, too, does palpation in the wound by the surgeon's finger. The evils of the latter procedure, however, are overbalanced by the advantages of a degree of diagnostic accuracy that cannot be attained in any other way. Although irrigation of the wound of a compound fracture of the skull is advised by many and countenanced by tradition, I am convinced that this is a dangerous procedure, whether done before or at operation. Moreover, since the same end can be accomplished in other and less dangerous ways, it has no justification in itself. The object of any irrigation is to direct a stream of fluid against the sides and bottom of a cavity with the intention of loosening unwanted debris from these areas, so that the stream returning from the depths of the wound will carry this material outside and away from the site of the injury. The greater the force

In the skull, however, the circumstances are radically different, since any compound fracture necessarily communicates with one or more of the intracranial meningeal spaces. These are only locally contaminated at the time of the infliction of the wound. Irrigation of such a wound inevitably leads to the deposition of some of the irrigating fluid—loaded with debris and contaminating organisms—in hitherto uninvolved and uncontaminated meningeal spaces (Fig. 1). The greater the amount and the stronger the flow of the irrigating fluid, the wider the contamination. That this is a real and not a theoretical danger is recognized even by the advocates of irrigation. They one and all advise that the irrigation be gentle. No matter how gentle it is, however, the fluid of necessity seeps into areas that would not have become involved had no fluid been used.

It is also argued that in these wounds—especially at the time of operation—the meningeal spaces are mechanically closed by the swollen brain. This may be so macroscopically, although watertight closure is extremely unlikely under such circumstances, but it is certainly not so microscopically. Since the spread of contamination is by

micro-organisms, macroscopic closure is of little importance. Furthermore, because the danger of irrigation lies in the flow of fluid and the benefits in the outgoing current, any procedure that does away with the former while retaining the latter is not only an acceptable substitute but is preferable. Such a procedure is found in suction. Here the movement of the débris is entirely outward; its removal is positive and under the constant and direct control of the operator, and is capable of being carried out through the medium of various-sized suction tips that may, if necessary, be either smaller than the smallest practical rubber catheter or as large as the occasion demands. A variation in the strength of the suction governs the amount of tissue that can be removed. By reducing the intracranial pressure by means of lumbar cerebrospinal-fluid drainage during operation, as suggested by Cone,¹¹ the edges of the brain wound separate and gape. Exposure is improved, bleeding vessels can be held in the sucker mouth until closed, and the procedure, being technically simple, is more effective than irrigation. Certainly there can never be a reason sufficient to justify irrigation of a compound fracture of the skull previous to complete débridement, and in my hands and on theoretical grounds it has been and is not only unnecessarily dangerous but also inefficient, when compared to suction alone at the time of the complete débridement.

The other important cause of unnecessary spread of contamination beyond the wound is found in the method of applying the first dressing. It is not necessary to re-emphasize the dangers that go with manipulation and the advantages that accrue to the patient through lack of handling of the wound. It has been my custom to limit the first dressing to the application of one or more sterile gauze pads to the wound. These are held in place with a bandage. Until such time as the patient is anesthetized and about to be subjected to a major débridement, all such procedures as cutting the hair, shaving the scalp, washing or wiping the wound, removal of foreign bodies or fragments of bone, ligation of all except the superficial temporal and great occipital arteries, and retraction of the wound edges have been rigorously avoided.

With the advent of the sulfonamides and the recognition of their great value as bacteriostatic agents when powdered into a wound, I shall in the future permit sufficient cutting of the hair and wiping of the surface of the wound to allow for a reasonably efficient application of the powdered form of one of this group of drugs to and around the wound at the first dressing. Shaving of the

scalp and washing of the wound at the first dressing, however, even when combined with chemotherapy locally, as advocated by Cloward,¹² are in my opinion contrary to all logic and cannot be too strongly condemned. In the necessary absence of figures, the good results that Cloward reports must be looked on as having occurred in spite of rather than because of this first aid.

It was intended that this entire series of 218 patients with compound fractures of the skull should be treated according to one technic.^{13, 14} All the patients were supposed to have been operated on as soon as their general condition would permit it to be done safely, and in any event within forty-eight hours of the infliction of the injury. As a result, the majority of operations were performed within twenty-four to thirty-six hours. The first dressing was supposed to have been as described above. The débridement was done in the operating room with the patient usually under a general anesthetic, such as ether by inhalation or Pentothal intravenously. As a rule, local anesthesia was not suitable because of the type of patients that makes up my clinic. The whole head was clipped and shaved, scrubbed for ten minutes with soap and water, washed with alcohol and then ether, and the scalp painted with a 0.2 per cent alcoholic solution of iodine after the patient had been placed on the operating table. The wound, which had been closed by sterile gauze during this preparation, was then cultured, often from several levels, after which it was thoroughly swabbed inside with 7 per cent tincture of iodine. Two teams of assistants were used. One team helped the surgeon do the débridement. The other — usually made up of two men — inserted a cannula into an ankle vein. This was kept open by dripping through it a 5 per cent solution of glucose in physiologic saline solution. Intravenous medication or an anesthetic was given when necessary by puncture of the rubber tubing of this apparatus. This team also collected blood for transfusion from donors and, by substituting this blood or plasma for the glucose solution, took care of any emergencies, such as surgical shock or hemorrhage, that arose in the course of the débridement.

The line of the incisions to be used was then scratched on the scalp, drapes were put in place, and the scalp and periosteal wound edges were excised *en bloc*, the instruments that were used in this excision being discarded. The bone was drilled in what was thought to be an uncontaminated area adjacent to the fracture line and the contaminated part of the fracture was cut loose, if possible in one piece, with the aid of a De Vilbiss rongeur. If the dura was intact and there was no reason to suspect the presence of a subdural

hematoma, it was not touched. If such a clot was suspected, however, the dura was opened without hesitation and the subdural space explored. Extradural hematomas were removed, and the source of the bleeding identified and closed. Tears in the venous sinuses were closed with muscle stamp grafts. If the dura was torn, its torn edges were excised, the tear being extended when necessary to expose properly the underlying cortex. Cortical lacerations and hematomas were removed by suction until all macerated brain tissue had been excised. Bullet tracts were cleaned of bone fragments as well as débris and followed down to the bullet, the latter being removed. In 1 patient, the bullet was found in the lateral ventricle. Intra-cortical hemostasis was attained by silver clips, the use of the coagulating current or muscle stamp grafts. No irrigation of any kind was permitted at any time. The dura was then closed over the cortical scar, making a relaxing incision laterally if necessary. Periosteum was used as a dural graft a few times, but fascia lata was not. The removed bone even if of large size was not replaced.

The scalp was closed tightly with two layers of interrupted silk stitches—one in the galea and one in the skin. The skin was scarified adjacent to all skin sutures deeply enough to draw blood, particular attention being paid to the corners. Mattress sutures of silkworm gut were occasionally used as tension sutures. All suturing was done from the periphery toward the center of the wound, and plastic types of scalp closure were used whenever necessary. No drain or pack was used in simple compound fractures.

Compound fractures involving the paranasal sinuses were prepared and débrided similarly but were drained by a Mosher copper-wire cone drain, iodoform gauze and boric-ointment gauze strips. Patients with cerebrospinal fluid rhinorrhea were operated on by way of a Frazier type of right frontal flap, which has been described elsewhere.¹⁴

As a means of measuring the efficacy of this technic, I have eliminated from this series all those patients whose death or postoperative sepsis could be directly traced to errors in carrying it out. For the same reason, the patients who died before being operated on have also been eliminated.

As already stated, there were 60 deaths (Table 2). The causes were as follows: surgical shock, 28 cases; circulatory failure, 5; the cerebral condition, 6; meningitis, 13; cortical abscess, 3; pneumonia, 1; gas-bacillus infection of the leg, 1; acute edema of the glottis, 1; transection of the cervical cord, 1; and an unknown cause, 1. Of these deaths, 1 from circulatory failure, 3 from cortical abscess and 6 from meningitis can be elim-

inated because of gross technical errors of therapy. Thus, the deaths can be reduced by 10 to 50 and the mortality from 28 to 23 per cent.

As stated above, 159 patients were operated on and 25 of these died. Thirty-nine cases (25 per cent) were classed as septic following operation. If 29 patients whose death or sepsis was traced to technical errors are eliminated, 130 patients may be considered as having been properly operated on. Twelve of these died, reducing the operative mortality from 15.7 to 9.2 per cent. Ten patients (7.6 per cent) developed postoperative sepsis that could not be accounted for by any error in technic. Thus, this mortality rate (9.2 per cent) and this rate of postoperative sepsis (7.6 per cent) must be considered as being inherent in the operative technic as outlined above. These figures must be improved by the use of chemotherapy if the latter procedure is to justify itself.

There can be no question of the value of any of the sulfonamide drugs as bacteriostatic agents when powdered into the usual wound, either with or without additional oral administration. Moreover, there is no evidence that, when these drugs are used intelligently and in reasonable amounts, any harm comes to the tissues locally or to the patient in general. It has been assumed that what holds true for usual wounds also holds true for craniocerebral wounds. Recent work, however, suggests that this conclusion is not justified and that unexpected and unpleasant side effects may follow the use of certain of the compounds, and that care must be exercised in the amount used of all of them. Hurteau,¹⁵ working with cats, demonstrated that following local application to a cerebral wound sulfanilamide was the most rapidly absorbed, sulfathiazole second, sulfadiazine third, and sulfapyridine the least rapidly absorbed. Furthermore, sulfadiazine exercised no untoward effect on the final result of wound healing and caused only negligible foreign-body reaction in the meninges. Butterell, Carmichael and Cone¹⁶ also worked with cats and applied the sulfonamide drugs to the cut surfaces of a cerebral wound. Their experiments indicated that the intensity and duration of the inflammatory reaction depended on the quantity of the drug used, its solubility and the length of time it remained in the wound. They also observed no undesirable side effects on nerve cells, neuroglia or myelin at a distance from the drugs and stated that the reaction remained local. As a result of their experiments they have not hesitated to use sulfonamides in wounds of the human brain but have used them circumspectly. They further state that they will continue to use them guardedly even when their local bac-

teriostatic and bacteriolytic action is proved beyond doubt, "for they do act also as foreign bodies." The implantation of the drugs in the ventricle did not alter their findings.

More recently Watt and Alexander¹⁷ report epilepsy following the use of sulfathiazole in the wounds of 5 patients on whom frontal craniotomies were performed. The drug was in contact only with the surface of the cerebrum. As a result of this experience, they applied the compound on the surface of the cerebrum in 10 cats. Nine developed epilepsy. Sulfadiazine (in 2 cats) and sulfacetamide (in 3 cats) were used in a similar fashion without producing any cerebral symptoms. It is to be noted that in both their clinical cases and experimental animals it was sulfathiazole that produced the epilepsy, and that furthermore, in contradistinction to the experimental work reported above, the drug was applied to the intact cerebral surface and not to the cut edges of a subcortical laceration. Pilcher et al.¹⁸ have had similar experiences in experimental dogs and a few cats with this same drug, and have also noted the increased toxic effect when the drug was applied to the unbroken cerebral surface as opposed to the cut surfaces. Ingraham and Alexander¹⁹ state that sulfadiazine powder can be safely used when the brain is not severely damaged, but suggest that further work must be done to arrive at a definite conclusion.

In 1 of my cases included herewith, sulfanilamide powder was used in the wound and sulfapyridine by mouth. No surgery was performed. The wound granulated, and when explored at the end of two weeks because of failure to heal was found to contain a "rock" of sulfanilamide. This was removed, after which the wound healed promptly.

In so far as the available evidence indicates, then, sulfathiazole should not be used in craniocerebral wounds. Sulfanilamide may be expected to give a high concentration of the drug for a short time, and sulfadiazine a lower concentration for a longer time. The evidence concerning the toxicity of sulfapyridine in craniocerebral wounds is inconclusive, and as a result, this drug should not yet be employed in such wounds. Care should be taken to use only the amounts of powdered crystals that are necessary, because it is evident that the powder acts as a foreign body when used in craniocerebral wounds, and may actually impede healing through creating a foreign-body reaction, in spite of the absence of any bacterial contamination.

Efforts directed toward lowering the mortality and the percentage of postoperative sepsis arising

out of compound fractures of the skull through the use of sulfonamide products should be concentrated on the use of either powdered sulfanilamide or sulfadiazine crystals, applied in and around the wound at the first dressing and at the débridement. Sulfathiazole should never be used, and sulfapyridine only in the absence of any of the other forms. The crystals should be powdered and applied to the wound surface by an insufflator. No more than a thin layer of the drug should be applied. This chemotherapy is not and cannot be a substitute for properly conceived surgery in the treatment of compound fractures of the skull. It is an adjunct to such surgery, valuable without doubt but entirely incapable of replacing the latter.

SUMMARY

An analysis of 218 cases of all types of compound fractures of the skull is presented from the point of view of complicating major injuries, age and gross, operative and nonoperative mortality.

Four principles are described as fundamental in the surgical therapy of compound fractures of the skull. They are as follows: All such wounds must be completely débrided within forty-eight hours of the time of infliction of the injury or else not operated on until completely healed for six to eight months. No patient should be operated on until he is out of surgical shock and until his general condition warrants it. After the diagnosis has been made by palpation through the wound, the first and only dressing prior to débridement must be one that can be applied with an absolute minimum of handling of the wound. Lastly, the débridement should be complete except in certain special fractures, it must be done in such a way as to avoid the spreading of bacterial contamination throughout the wound and the production of tissue necrosis, it should include the removal of all large foreign bodies, and no wound that has been properly débrided either needs to or should be drained.

A detailed discussion of the technic of the débridement is given. Irrigation of the wound before and during operation is condemned and the reasons therefor are given.

Chemotherapy in the form of sulfanilamide or sulfadiazine is recommended both by mouth and in the wound, but only as an adjunct to properly conceived and executed surgery. Sulfathiazole should not be used in craniocerebral wounds.

With therapy based on the above principles and without the use of chemotherapy, and with débridement done according to the above technic, the mortality in 130 patients who had been prop-

erly operated on was 9.2 per cent and the rate of postoperative sepsis was 7.6 per cent.

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SPINA BIFIDA AND CRANIUM BIFIDUM*

III. Occult Spinal Disorders

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ROUGHLY 25 per cent of normal children have occult defects in the vertebral laminae and this incomplete closure is frequently demonstrated in x-ray films taken for some other reason. The defect is likeliest to occur in the lumbar or sacral region and can be shown to have persisted in many normal adults. Over a twelve-year period at the Children's Hospital we have selected the much smaller group of patients who have had symptoms associated with occult spina bifida. Probably too few of these patients have been given the benefit of local exploration, but it is only by careful study and selection that operation can be offered to the proper group.

The variations of symptoms and physical findings are unlimited. In some cases there may be such faulty development of the lower portion of the spine and cauda equina that surgical treatment will not be helpful, and those patients who might possibly be worse after operation must be carefully excluded.

PRESENTING SYMPTOMS AND SIGNS

Of the 65 cases studied, 31 were first seen in the orthopedic clinic and the most frequent presenting complaint was maldevelopment of the feet or lower extremities with some disturbance in gait, which was present in 29 cases. The findings in-

cluded valgus, varus and cavus deformities of a foot, a small foot and a limp due to muscle weakness. In the large majority of cases the deformity was unilateral. The second commonest complaint was some local abnormality, such as a swelling, a bony lump or defect, a scoliosis or a local overgrowth of hair. These accounted for 22 cases. Enuresis or incontinence brought 7 patients to the hospital. In 9 cases the spina bifida was an incidental finding.

The neurologic disabilities are not easily classified because of the difficulty of deciding whether or not a given abnormality is on a neurogenic basis. If a patient on physical examination shows anesthesia over the distribution of the fifth lumbar root and at operation is found to have a tumor pressing on that root, the cause and effect are apparent. In most of our cases, however, the findings at physical examination were various degrees of muscular weakness in a lower extremity and an abnormality of posture presumably dependent on this imbalance of muscle groups. The findings at operation suggest that the muscle weakness and imbalance may be on a neurogenic basis. The age group dealt with made neurologic examination difficult, but abnormal reflexes were recorded in 15 cases, a positive Babinski response in 7, poor sphincter tone in 6, and abnormal sensation in the lower extremities in 5.

Besides the neurologic or developmental changes in the lower extremities, which may or may not have been produced by lesions of the cord or

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cauda equina at the site of the spina bifida, there were a few local findings of importance. As determined by physical examination or x-ray or both, the lesion was present most frequently in the lumbosacral region (25 cases). Eighteen cases showed sacral involvement alone, 4 dorsal, 3 dorso-lumbar and sacral, 3 dorsolumbar, 1 cervicodorsal, and 1 cervical.

As stated above, some local abnormality, such as a soft or bony swelling, a local overgrowth of

might cause a disturbance in gait. In 15 cases, there was no local visible or palpable abnormality that would suggest the spinal defect.

OPERATED CASES

Of the 65 cases reported, 26 had exploration of the region of the spina bifida. In 4 of these, the procedure was minor in nature and consisted only in local excision of a subcutaneous lipoma or dermoid, or incision and drainage of an infected

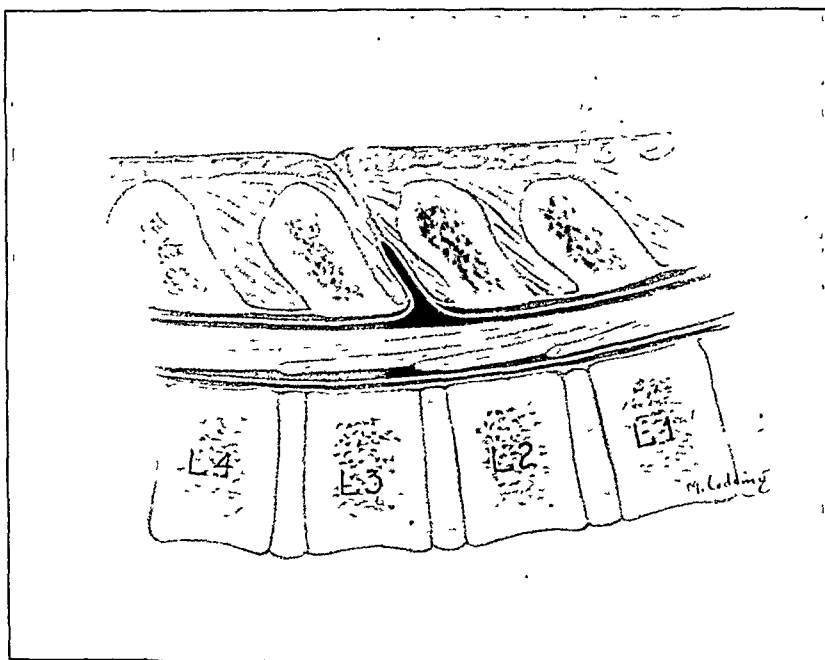


FIGURE 1. *Fibrous Stalk Connecting Dimpled Area in Skin with a Protrusion of the Dura between Laminas.*

hair or a palpable defect, was the presenting complaint in 22 cases. Routine physical examination showed a palpable bony defect in 28 cases, and a local overgrowth of hair in 14. Of these 65 cases, in 13 the abnormality was associated with a so-called "lipoma." As described in a previous paper,¹ lobules of gritty, firm fat, bound together by fibrous septa, usually adherent to adjacent fascial (or dural) planes by firm and often vascular attachments are frequently found associated with spina bifida. They may be at any tissue level from the cord itself to the subcutaneous tissue or may extend directly from one layer to another, binding the various tissues together and thereby producing adhesions and preventing the normal movement of the caudal end of the spinal cord with growth.

It should be emphasized, however, that spina bifida may be present without any symptoms or signs. It was present in 11 cases without any neurologic disability or abnormality of the lower extremities, such as valgus or small foot, that

dermoid. In 22 cases, a laminectomy was performed. One of these was in a five-day-old infant with bilateral brachial palsy. At operation acute angulation of the cord due to hemivertebras was found. The patient died two days after operation. Eliminating this case as being unusual and complicated by the other vertebral anomalies in addition to the spina bifida, there were 21 cases. Some of these patients had two-stage operations. Many of them had previous or subsequent orthopedic operations to correct the deformities of the extremities.

The findings at operation were variable. The most frequent finding was a combined intradural and extradural lipoma, which was present in 5 cases. Three cases showed extradural lipoma, 3 a fibrous tract leading from the skin to the dura, 2 subdural lipoma, 2 extradural lipoma with a bifid spinal cord, 2 no gross lesion of the spinal cord or the nerve roots, 1 an abnormal spicule of bone with pressure on the nerve roots, 1 a fibrous tract from the skin to the ligamentum flavum,

1 a constriction of the cord due to adhesions, and 1 a meningocele entirely contained within the sacral canal.

The criteria on which success of operations of this sort must be based are difficult to determine

operation in 13 cases. In 3 cases the cord or roots showed an abnormality and the disturbance in gait persisted. Three cases have not been followed long enough to determine the result, although all these showed obvious disease at oper-

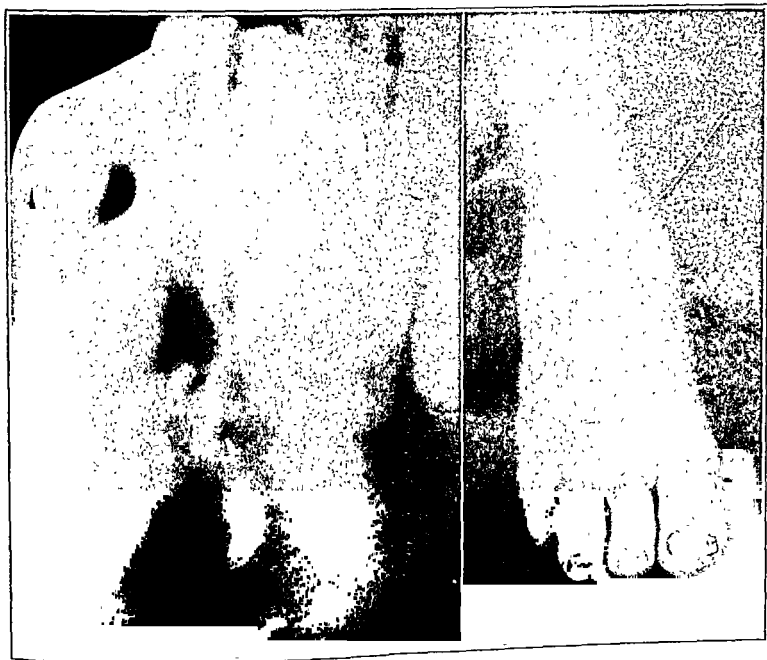


FIGURE 2. Case 2.

The photograph on the left shows the abnormal prominence of a spinous process and dimpling of the skin over the second lumbar vertebra; that on the right, the trophic ulcer of the toe.

because of the multiple complaints. Also, where permanent nerve damage has been present it is not possible to expect improvement. It therefore seems justifiable to consider a result as good if a definite cause of progressive symptoms can be found and relieved and if no further progression of symptoms occurs.

There was no operative mortality in these cases. In some cases there was striking recovery, such as healing of a trophic ulcer with return of sensation, or marked improvement in urinary and fecal control. It is important that patients who are developing equinus or cavus deformities be operated on early, because such deformities once present cannot be expected to disappear following operation. Using the criteria defined it can be said that a good result was obtained

in one case. One showed a bifid spinal cord. One patient (Fig. 1) operated on because of incontinence, with the finding of a fibrous cord from the subcutaneous tissue to the dura, exerting tension on the latter, showed improvement in the hospital but lapsed to practically her preoperative state when left with unco-operative parents. One patient awaits reoperation because complete removal of an extradural lipoma was not possible at the first operation.

CASE REPORTS

CASE 1 (C. H. 75872). This patient was first seen in the hospital at 2 months of age because of bilateral club feet. The feet were treated with manipulation and then casts. At the age of 4 he was admitted because of a trophic ulcer of the right small toe (Fig. 2). This ulcer healed and the toe was amputated. Spina

was noted at that time. He was followed in the Out Patient Department and did fairly well except for occasional trophic ulcers. At the age of 8 he had a right arthrodesis for persistent varus deformity of the right foot. At that admission reflexes in the right leg were absent and there was diminished sensation over the lower half of the lateral surface of the lower leg and the dorsum and sole of the foot. At 11 years of age the patient was admitted for a trophic ulcer of the right fourth toe, which subsided following treatment with wet packs.

CASE 2 (C. H. 263163). This girl first entered the hospital on the Neurological Service at 9 years of age with a chief complaint of progressive talipes equinovarus deformity of both feet of 4 years' duration. The feet tended to become cold. Otherwise there were no complaints. The patient had had treatment with corrective shoes and arch supports without relief. The family and past histories were not remarkable.

Physical examination showed diffuse mottling of both lower extremities, with atrophy of the legs from the knees

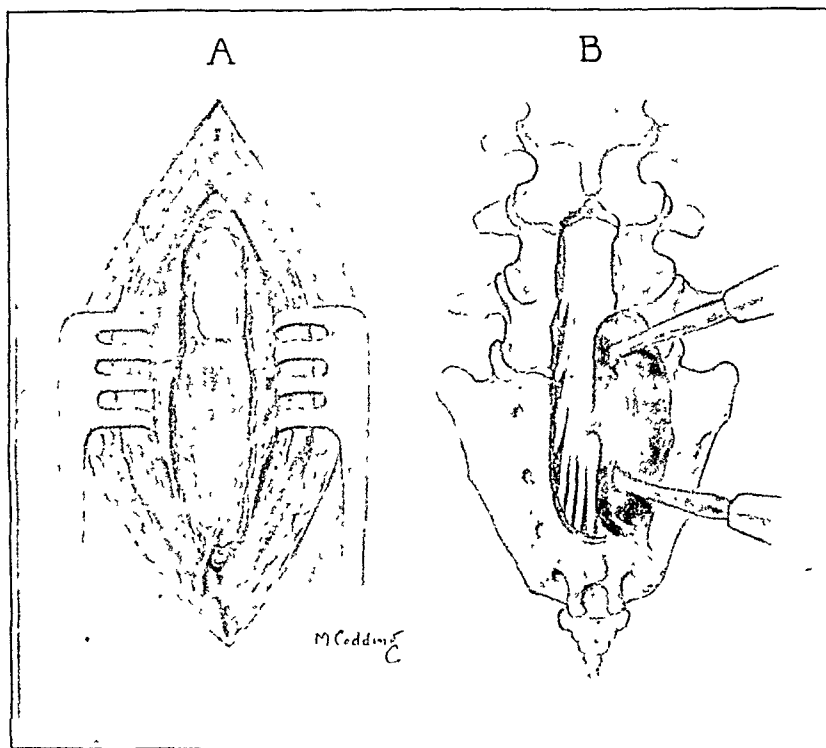


FIGURE 3. Case 2.

These drawings show the intraspinal meningocele connected with the dura by a small stalk.

Four months later he was admitted for a trophic ulcer of the right third toe that had developed cellulitis.

Physical examination showed a large crater over the third toe discharging purulent material, with surrounding cellulitis. The diminished sensation over the lower leg and foot was still present, with absent temperature sense. The spine showed a dorsal angulation over the 2nd lumbar vertebra with a palpable bony defect. X-ray examination showed abnormal development of the 12th dorsal vertebra and all the lumbar and sacral laminae, with incompletely formed, defective and incompletely fused arches. It was decided that there might be pressure on the spinal cord associated with the spina bifida, so laminectomy was carried out. On opening the dura definite constriction of the cord due to adhesions associated with the defective closure of the spinal cord was found at the level of the 11th dorsal vertebra. The cord was freed at that point.

Postoperative recovery was uneventful. A small piece of bone was removed from the base of the ulcer 7 days postoperatively, following which healing rapidly occurred. Postoperatively there was return of sensation and improvement in control of the anal sphincter. When the patient was last seen, 10 months after operation, his toes were still in good condition.

down, talipes equinovarus deformity of the feet and thick calluses on the toes. Neurologic examination was negative except for diminution of pain and touch sensation in the toes bilaterally. X-ray films of the spine showed a spina bifida of the 3rd lumbar vertebra and of the sacral segments, with a poorly formed sacrum.

Laminectomy was performed in two stages owing to the extensive dissection necessary, and a meningocele (Fig. 3) was found extending from the lumbosacral junction through the sacral canal to the undersurface of a dimple in the skin just above the anus. The sac contained dark-yellow fluid. No connection with the dura proper could be demonstrated except for a tiny fibrous stalk. The sac was freed from the nerve roots and excised.

Postoperatively the patient did well. Six months after operation she showed return of sensation to the toes, and the temperature of the lower legs seemed normal. She walked better than before the operation. Muscle examination showed essentially the same picture as preoperatively.

CASE 3 (C. H. 244120). This girl was first seen in the Orthopedic Clinic at 9 years of age for a deformed left foot, which had been present at birth.

Physical examination showed atrophy of the left lower leg and equinovarus deformity of the foot, associated with a cock up of the toes (Fig. 4). The left foot was considerably smaller than the right and there was some diminished sensation over it. The spinous process of the 3rd lumbar vertebra appeared double. X-ray examination

The patient had a smooth postoperative course and was discharged home on the 16th postoperative day immobilized in a plaster jacket. At the time of discharge the area of hypoesthesia had diminished so that instead of half the dorsum of the left foot only the toes of the left foot were affected. Muscle examinations before opera-

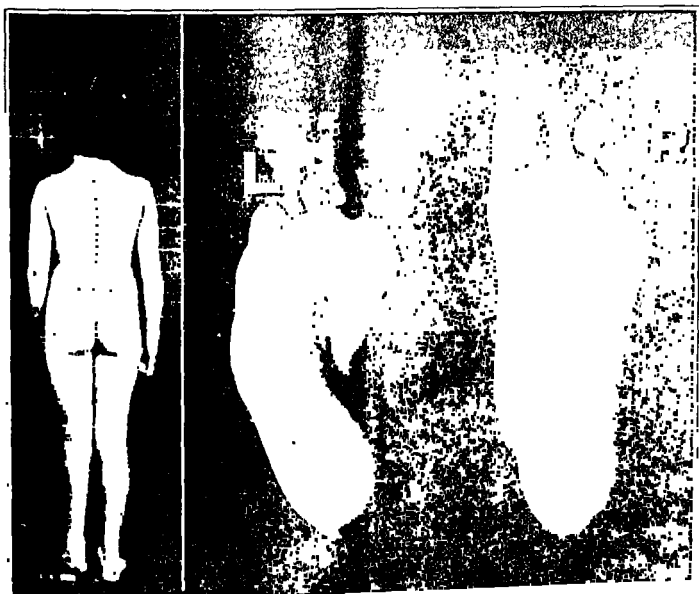


FIGURE 4 Case 3

The photograph on the left shows the short left leg and atrophy of the muscles of the calf; that on the right, the deformity of the left foot, as seen from below.

showed congenital anomalies of the laminae of the 2nd and 3rd lumbar vertebrae, with partial fusion of the laminae and indentation of the posterior aspects of the vertebral bodies. There were also defects in the laminae of the 5th lumbar vertebra and the 1st sacral segment.

Lumbar puncture was done, with normal spinal fluid findings, and the patient was discharged home. She was followed in the Out Patient Department over the next year and developed further loss of sensation in the left foot and also loss of reflexes on the left. Lumbar laminectomy was therefore carried out. A lipoid mass was found in the subcutaneous tissue, and extending from this was a fibrous stalk that penetrated the edge of the 3rd lumbar vertebra and entered the neural canal, but without any connection with the dura (Fig. 5). On opening the dura, small swellings giving the appearance of neuromas, the maximum being twice the diameter of the nerve trunk, were seen on the 2nd, 3rd and 4th lumbar roots. These swellings could not be isolated and no attempt was made to resect them. The canal was left wide open.

tion and 5 months postoperatively showed no change in muscle strength.

CASE 4 (C. H. 239250). This girl was first seen in the Orthopedic Clinic at 5 years of age, with a complaint of weakness of the left foot. Five months previously it had first been noted that the left foot was smaller than the right and that the patient seemed to drag it while walking. These complaints had progressed to entry.

Physical examination was normal except for the spine and lower extremities. There was a growth of long, dark hair over the lower lumbar and upper sacral segments, with a suggestive underlying spinal defect (Fig. 6). The left foot was smaller than the right and showed a cavus deformity. The left calf was 0.5 cm. and the left thigh 10 cm. smaller than the right. Reflexes and sensation were normal in both lower extremities. X-ray films showed defects involving the laminae of the first three lumbar and upper sacral segments, with widening of the interpeduncular spaces. The spinal fluid was normal.

At laminectomy it was found that the spinous processes of the 3rd and 4th lumbar vertebrae were absent.

that the laminae were overlapped, those on the right lying under the left so as to cause constriction of the dura

left, in the dura at the level of the 4th interspace, there was a funnel-shaped depression that was attached to a

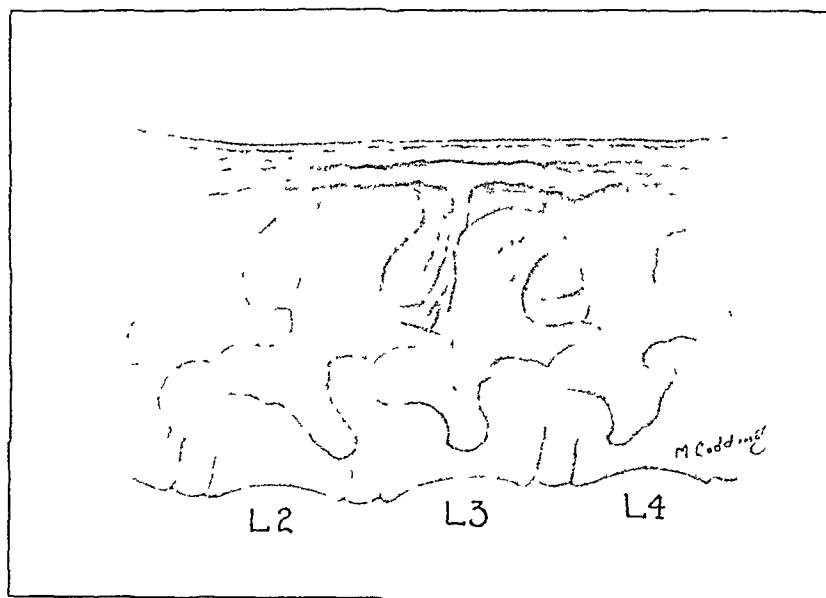


FIGURE 5. Case 3.

This drawing is a reconstruction of the firm lipoma extending from the dura to the subcutaneous tissue.

and absence of epidural fat. The dura was exposed and opened, and chronic arachnoiditis was found. On the

piece of bone coming from the ventral surface. The nerve roots on the left were deflected by this bone and were adherent to it. The nerve roots were freed, and the bony prominence removed.

Postoperatively the patient made a good recovery and was discharged in a plaster jacket on the 14th postoperative day. With orthopedic shoes she did well. The gait was better and the deformity did not progress.

SUMMARY

An analysis of 65 cases of spina bifida occulta is presented. The symptoms and usual findings are listed.

Twenty-one cases in which laminectomy was performed are discussed, and the operative findings summarized.

The indications for operation were specific, and operation was not performed without a definite history of progressive difficulty.

In only 2 out of the 21 cases did operation fail to show a lesion that might account for the presenting complaint. In the large majority operation showed a definite lesion affecting the cauda equina or nerve roots, that could be remedied surgically.

The findings suggest that probably more of the questionable cases should be offered the benefit of exploration.

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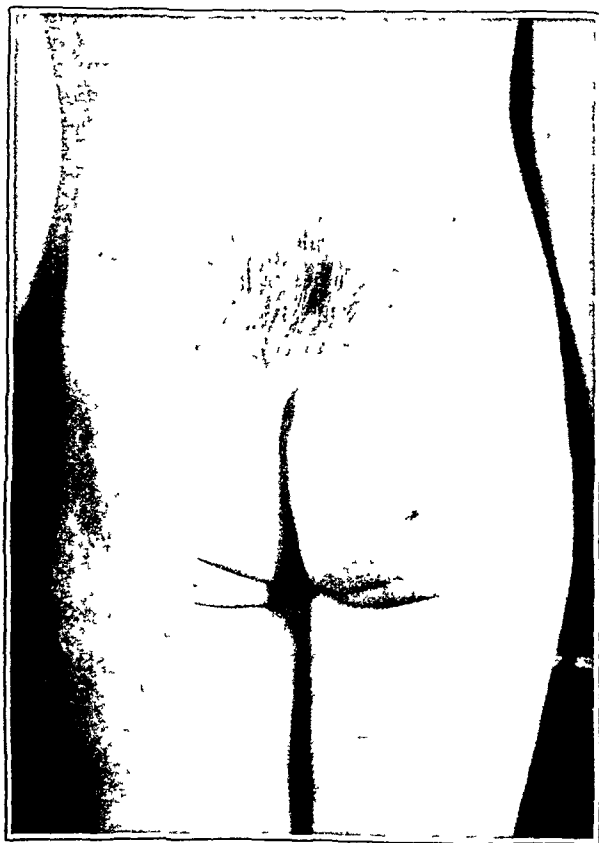


FIGURE 6. Case 4.

This photograph shows the abnormal growth of hair over the site of the spina bifida.

RESECTION OF THE BLADDER NECK FOR OBSTRUCTION IN WOMEN

Report of a Case

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OBSTRUCTION of the vesical neck in females as compared with that in males occurs infrequently. Young,¹ who reviewed the literature in 1938, was able to find only 36 cases in females. The condition is undoubtedly commoner than this figure suggests, and the smallness of the figure must be attributed to lack of recognition of cases on the one hand, and failure to report recognized cases on the other. In any event, obstruction in females is a rarer event than in males, and the basic cause is to be found in the simpler structure of the female urethra (Lewis²). This simpler structure does not predispose the female urethra to the frequency and to the degree of inflammatory lesions that may lead to sclerotic changes at the bladder neck.

That the female urethra is the embryologic homologue of the portion of the male urethra that lies between the vesical orifice and the prostatic utricle was well shown by Johnson³ in 1922. By means of wax reproductions of the urethras of female embryos, he demonstrated that the female urethra contained branching urethral glands that he believed to be homologous to the male prostate. These glands may become infected and result in a condition equivalent to the chronic prostatitis observed in the male.

Young,⁴ in his recent book on genital abnormalities, has reported a case in which the female urethral glands had developed in size to a point approaching that of the male prostate. There was a hyperplasia of the adrenal cortex, giving rise to a masculinizing effect due to the increase of androgenic substance. The female urethra may therefore be the seat of the same type of disease as that observed in the male. Thus, there can be chronic infection of the glands,—corresponding to chronic prostatitis,—fibrosis with a median bar or contracture of the neck of the bladder, and finally, in cases of glandular dyscrasia, adenoma of the male can be simulated. Furthermore, these conditions probably arise from the same causes as they do in the male, whatever those causes may be.

Caulk,⁵ in 1921, first called attention to bladder-neck obstruction in females, which he treated successfully by means of his punch. He believed that the obstruction was due to fibrosis and hyperplasia

at the bladder neck resulting from three causes: inflammation; trauma at childbirth and trauma from sexual activity.

Young¹ suggested that when the female urethra became infected, the urethral glands caused infection to persist, subsequently leading to fibrosis. Thompson,⁶ who reported 24 cases of vesical dysfunction in females, agreed that chronic inflammation was the most important cause, but added that in some cases there was an additional factor in the form of nervous imbalance between the sphincter (parasympathetic innervation) and the detrusor muscle (sympathetic innervation), which led to spasm of the sphincter and subsequent hypertrophy and hyperplasia of the muscle.

In considering the etiology of bladder-neck obstruction in females, the common denominator appears to be chronic inflammation in the form of a nonpurulent urethritis.

The symptoms of obstruction in females are precisely the same as those observed in males, namely, hesitation of the stream, difficulty in starting it, its slowness and so on, leading to complete retention. The cystoscopic picture, like the symptoms, is strikingly similar in both sexes, with marked trabeculation and sacculation, and in advanced cases, the accumulation of residual urine. The cystoscopic picture at the bladder neck, however, may be quite unrevealing, showing only a minimal amount of tissue in the form of a ridge or bar, which, taken alone, is not sufficient for diagnosis. In making the diagnosis it is necessary to take into account the secondary signs of obstruction, which are to be found in the bladder and in the upper urinary tract and which take the form of dilatation due to back pressure. The presence of residual urine is important.

In the treatment of this condition, as the following case well illustrates, the passage of sounds, even those of large caliber, is not sufficient to control the situation. Where the lesion is a localized stricture of the urethra, the passage of sounds constitutes adequate treatment, as it does in the male. To quote Kelly,⁷ "If there is much infiltration above the localized stricture area making restoration of the tissues a hopeless task, one may then make an annular resection of the urethra, cutting out the diseased parts." Kelly thus recognized that certain types of obstruction of the

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female bladder neck do not respond to simple dilatation. The case to be presented demonstrates this very well, for previous to operation, sounds were passed to little or no effect. The treatment of this condition in females, therefore, as in males, is transurethral resection, and rarely does one ever have to do so little to achieve so much. The making of several incisions with the removal of the corresponding number of pieces of tissue is all that is necessary. Because the female urethra lies on the superior vaginal wall throughout its course, great care must be taken to avoid cutting too deeply and thus causing the formation of a vesicovaginal fistula.

The matter of incontinence following resection of the bladder neck appears to be important only in theory, for in practice, incontinence was observed by none of the authors reporting punch and electrical-resection operations. Because obstruction in the female is accompanied by the same impairment of renal function as in the male, pre-operative catheter drainage is as necessary in the former as in the latter.

CASE REPORT

S S, a 54-year-old, married woman, was seen in November, 1940, 4 days after an attack of acute retention. There was a history of difficult urination of 16 years' duration, culminating in acute retention. The patient had had two children, each labor not being unduly dif-



FIGURE 1. *Anteroposterior Cystogram Showing Enormous Dilatation of the Bladder and Two Large Diverticula.*

ficult so far as she could recall. There was nothing to suggest a previous infection of the urethra. She was first seen in the office, where the urethra was dilated by means of sounds (up to No. 28 Fr.) and a catheter was passed to the bladder. About 2000 cc. of cloudy urine was removed, although the patient had voided just before examination. A smear of the catheterized urine revealed many gram-negative bacilli, probably colon bacilli. The patient

was advised to go to the hospital, but because the passage of sounds had given some relief she did not do so until January, 1941.

At that time cystoscopy revealed a markedly dilated bladder containing over 2000 cc. of cloudy urine. The bladder wall was trabeculated and sacculated, and just behind the trigone were the openings to two large diverticula. At the bladder neck there was a moderate ridge or bar which, however, did not appear particularly

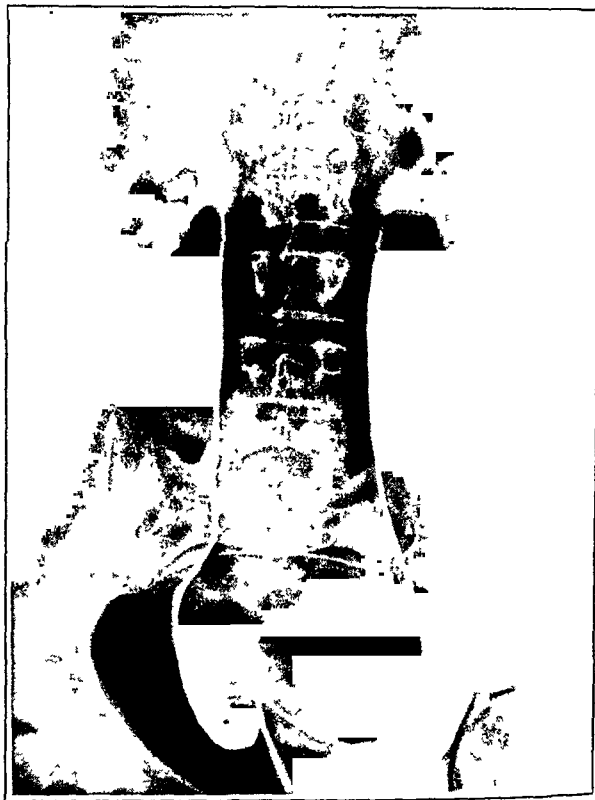


FIGURE 2. *Bilateral Pyelogram Showing Beginning Back-Pressure with Slight Dilatation of the Pelvis and Blunting of the Calyces on the Right.*

obstructive. A cystogram (Fig. 1) and a pyelogram (Fig. 2) confirmed the cystoscopic findings, and operation was decided on.

The nonprotein nitrogen on admission, interestingly enough, was 36 mg. per 100 cc., suggesting that the bladder had acted as an excellent buffer, protecting the upper urinary tract from the back pressure. With a Foley bag catheter in place a phenolsulfonephthalein function test was done. It showed 19 per cent excretion in the first 15 minutes and 13 per cent in the next 45 minutes, or a total of 32 per cent in 1 hour. The volume of urine excreted in 1 hour was 750 cc.

At operation the diverticula were removed; inspection of the internal orifice showed this to be high in position, but it admitted the tip of the index finger fairly easily. It was decided that the diverticulectomy, followed by periodic passage of sounds, would serve to control the situation.

The postoperative course was uneventful, except that before the suprapubic sinus became completely dry, a retention catheter had to be inserted and left in place for 2 days. The patient was discharged from the hospital

to be followed in the office. Her residual on discharge was 100 cc but over a period of 2 months it varied from 100 to 450 cc and was usually around 300 cc. The urine was infected and irrigations and the administration of sulfonamide drugs failed to clear up the infection. Accordingly the patient was told that she had an obstruction at the bladder neck that refused to respond sufficient

was nil and the urine was completely free of infection. A cystogram (Fig 4) revealed that the bladder capacity



FIGURE 3 Photograph of Section of Tissue Showing Exfoliated Fibrous and Absence of Glandular Elements

ly to dilatation and that it would be necessary for her to re-enter the hospital for operation.

The patient did so in April, 1941, and transurethral resection was done. Six cuts were made, with the removal of no more than 2 gm. of tissue (Fig 3). A retention catheter was inserted and left in place for 2 days and when this was removed the patient voided promptly and freely and emptied the bladder completely. The urine became free of infection in 10 days.

The patient was examined in April, 1942, 1 year after transurethral resection. At that time the residual urine



FIGURE 4 Anteroposterior Cystogram after Operation

was about 350 cc and that the bladder function was perfect.

SUMMARY

The pathology, etiology, symptoms and treatment of obstruction of the bladder neck in women are briefly discussed and a case is reported.

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MEDICAL PROGRESS

EPIDEMIOLOGIC ASPECTS OF FOOD-BORNE DISEASE

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A VAST variety of diseases may be transmitted through the medium of food, milk or water. Typhoid fever, paratyphoid fever, botulism and dysentery are classic examples of bacterial diseases that are transmitted to the unsuspecting consumer through the food and drink he ingests. A food-borne disease is an illness whose etiologic agent gains entrance to the body by the alimentary tract. In the past the term "food poisoning" has been applied conventionally to any acute gastroenteritis characterized by nausea, vomiting and diarrhea. However, a substantial portion of so-called "food poisoning" is not poisoning but an infection, and this term is therefore erroneous. "Ptomaine poisoning" is another misleading term often applied to an acute gastroenteritis. As a matter of fact, as is well stated by Whipple,¹ "ptomaine poisoning doesn't exist." Ptomaines are substances produced in the decomposition of food by bacteria. Examples of this type of decomposition are the ripening of game and wild fowl and the aging of cheese. None of these foods that are relatively high in ptomaines are poisonous.

CLASSIFICATION OF DISEASES

The food-borne diseases can be divided into two main groups: food infection, in which the etiologic agent is a living organism and the symptoms are the manifestation of the reaction of the host to its action; and food poisoning, in which the causative agent is a noxious substance that in itself is responsible for the characteristic clinical sequence, with or without the presence of a living organism.

The etiologic agent of food infection may be a virus, a bacteria, a protozoa or a helminth. By far the commonest agents are bacteria, chiefly the *Salmonella* and the *Shigella*. Trichinosis is perhaps the most prevalent type of helminth food infection, and amebiasis the commonest protozoan infection. An example of virus food-borne infection is infectious diarrhea of the newborn. The following food infections are reviewed in this paper: amebiasis, trichinosis, typhoid fever, para-

typhoid fever, bacillary dysentery, undulant fever, scarlet fever and septic sore throat.

Food poisons may be subdivided into two groups: endogenous poisons, which are usually present in the food, — for example, mushroom poisoning or oxalate poisoning from rhubarb leaves, — and exogenous poisons, which are not an integral part of the food but an addition to it. The exogenous poison may be an organic substance, such as the alkaloid derived from a flagellate, which at certain times of the year infests mussels, the toxin of *Clostridium botulinum* or the commonest type of food poison, the enterotoxin of a hemolytic *Staphylococcus aureus*. Poisoning from this group is often termed food intoxication, since the symptoms are usually due to a toxin. On the other hand, the exogenous poison may be an inorganic compound such as the residue of an insecticide spray on fruits or vegetables, the accidental addition of fluorine to food or the solution of cadmium from replated metal containers. This type of food poisoning is often called chemical poisoning. The types of poisoning to be reviewed here are staphylococcal enterotoxic poisoning, botulism and chemical poisoning.

SYMPTOMATOLOGY

In food infections, the incubation period varies from six hours to two weeks, with characteristic averages for the different types of organism. The shortest periods are encountered with *Salmonella* infections, but usually the incubation period of a food infection is longer than that of food poisoning. Whereas fever is a common symptom of food-borne infections, it is not a frequent finding in staphylococcal enterotoxic poisoning. Nausea, vomiting, abdominal cramps or pain and diarrhea, leading to prostration, are the usual rapid sequence in severe staphylococcal poisoning; chills, sweats and toxemia are other frequent symptoms. The duration is usually a matter of hours, and recovery is rapid. In *Salmonella* infection recovery is a matter of days. In the investigation of any suspected food-borne outbreak an analysis of the symptoms will often give the epidemiologist a clue to the etiologic agent. The shortest incubation periods are observed in some types of chemical food poisoning, where symptoms may occur in ten

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III. 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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minutes to several hours. The enterotoxin of *Staph aureus* produces symptoms in two to six hours, whereas *Salmonella* infection incubation averages six to twenty-four hours. Nausea or vomiting is not likely to occur in food infections with long incubation periods.

INVESTIGATION OF FOOD-BORNE OUTBREAKS

Having obtained a record of the symptoms of all the patients in a given outbreak, the next most important step is to obtain a dietary history from each. Dack² presents a questionnaire that may be particularly useful to physicians interested in the compensation and legal aspects of food poisoning. As soon as the investigator finds which foods are common to all cases, steps should be taken to prevent further cases. Thereafter a study of the vehicle can be made, determining its source, handling, storage and preparation, in an endeavor to ascertain the mode whereby the food became contaminated. Lastly, the etiologic agent is determined by laboratory examination of the food and of the vomitus and feces of patients and food handlers. A complete investigation can reconstruct the epidemic, step by step, from its source to the time of the investigation.

MODES OF CONTAMINATION OF FOOD

Food-borne infection may be due to animal disease transmitted through milk or meat directly to the consumer. Trichinosis is a classic example of animal disease transmitted through uncooked pork. *Brucella* and certain *Salmonella* and streptococcal infections are examples of bacterial diseases of animals transmitted to man. Food may be contaminated by flies, rats or mice, or by food handlers who are active cases or carriers and who soil their hands with saliva, urine or feces, thereby introducing the organisms into the food they handle. Infection of food with staphylococci may occur from boils, infected wounds or sore throats of food handlers. The storage of food is an important factor in the morbidity rate; the longer the infected food is kept in a warm place, the higher the attack rate. Vegetables may be infected with amebas by fertilizing the soil with human excreta. Botulism is caused by undestroyed spores of *Clostridium botulinum* derived from the soil. Chemicals may gain entrance to foods. An insecticide spray may be found on fruits or vegetables, roach powder, which contains fluorine, may be added to the food by mistake for flour or milk powder, or a solution in an acid medium of cadmium from replated food containers may contaminate their contents. Often the mode of infection of the food cannot be determined. Many food processing methods may be the means of introduc-

ing pathogenic organisms unless proper precautions are taken. Some of the outbreaks reviewed here illustrate the protean modes whereby food becomes the vehicle of food-borne disease.

PREVALENCE OF FOOD-BORNE DISEASE

The serious nature of gastroenteritis in military forces can be estimated from the incidence of this disease in the United States Army. During World War I, according to Dunham,³ 87,774 cases of enterocolitis and diarrhea were admitted to hospitals, with 195 deaths—an annual case rate of 21.26 per 1000 men. Undoubtedly there were many more cases that did not require hospitalization. The average time lost from duty was eleven days, a total of almost a million days in hospitalized cases alone. In 1934 and 1935 the rates of hospital admissions were 21.95 and 21.14 per 1000, respectively.

The German literature is full of accounts of bacillary dysentery among the German troops in Poland.⁴ Rodenwaldt⁵ states, "Dysentery is the most dangerous of war diseases not only because of its physical effects, but also because it has such a powerful demoralizing effect." During World War I, according to Wurm,⁶ there were 155,000 cases of dysentery in the German Army. During the invasion of Poland, in September, 1939, several outbreaks of bacillary dysentery occurred simultaneously. These outbreaks were due to different organisms and were therefore unconnected. The speed of the campaign forced troops to eat whatever they could lay their hands on, including a great deal of unripe fruit, and the heat made them drink water regardless of its purity. Strangely, there was no epidemic among the Polish prisoners or the civilian population. Many German troops had to be evacuated to the rear, where, because of unfavorable conditions and overcrowding, dysentery spread among the hospital personnel.

However, food-borne disease is prevalent in peacetime as well as wartime. In 1923, the United States Public Health Service began the collection of data on milk-borne disease.⁷ Prior to this date, knowledge of milk-borne outbreaks was limited to those reported in the literature. As shown by these surveys, the number of known milk-borne outbreaks in the United States increased from an average of 17 per year prior to 1923 to an average of 42 per year since that date. From 1938 to 1941, inclusive (Table 1) there were 163 outbreaks, with 6923 cases and 48 deaths. In 1938,⁸ there were 42 outbreaks, with 1587 cases and 27 deaths. All these outbreaks were due to raw milk or raw milk products, with the single exception of an outbreak traced to improperly pasteurized milk. In 1939, there were 41 outbreaks, with 2509 cases and 7

deaths.⁹ Thirty-seven of these were traced to raw milk and 4 to milk that became contaminated subsequent to pasteurization. In 1940, there were 43 outbreaks, with 1658 cases and 10 deaths.¹⁰ The largest of these was an epidemic of septic sore throat due to a hemolytic streptococcus at Digh-

TABLE 1. *Disease Outbreaks Conveyed through Milk and Milk Products in the United States, 1938-1941.**

DISEASE	No. OF OUTBREAKS	No. OF CASES	No. OF DEATHS
Diphtheria	2	36	3
Dysentery	9	813	0
Food poisoning:			
Staphylococcal	25	868	0
Other	22	522	0
Gastroenteritis	13	1326	0
Paratyphoid fever	2	24	0
Scarlet fever	11	187	1
Septic sore throat	18	2512	12
Typhoid fever	50	478	32
Undulant fever	8	119	0
Unknown	3	38	0
Totals	163	6923	48

*Assembled from data collected by the United States Public Health Service.⁹⁻¹¹

ton and Taunton, Massachusetts. Investigation revealed that members of the milk dealer's family were suffering from sore throats. The organism was spread by the raw milk; 284 cases and no deaths were reported. In 1941, there were 37 outbreaks, with 1049 cases and 4 deaths.¹¹ Again, raw milk and raw-milk products or pasteurized milk improperly handled were responsible for most of the outbreaks. The known responsible diseases, in order of number of cases, were septic sore throat, gastroenteritis, staphylococcal food poisoning, undulant fever, diphtheria and paratyphoid fever.

Dublin, Rogers, Perkins and Graves¹² studied milk-borne outbreaks in upstate New York from 1917 to 1941. During these twenty-four years there were 168 outbreaks, with 9982 cases, of which 6812 were septic sore throat and scarlet fever, 1423 gastroenteritis, 1209 typhoid or paratyphoid fever, 411 bacillary dysentery, 123 diphtheria, and 4 poliomyelitis. Feemster¹³ reported on the prevalence of milk-borne disease in Massachusetts from 1933 to 1940; there were 6 outbreaks, with 469 cases. Four outbreaks were of scarlet fever or septic sore throat (412 cases), 2 of undulant fever (12 cases), and 1 of gastroenteritis (35 cases). This is the smallest number of outbreaks recorded for any similar period in Massachusetts. According to Getting,¹⁴ in 1931 65 per cent of the population of Massachusetts lived in communities with regulations requiring the pasteurization or certification of milk. By 1940, 80 per cent of the population were living in these communities, and Feemster¹³ states that over 90 per cent of the milk consumed

in Massachusetts was pasteurized. Undoubtedly this increase in pasteurization is responsible for the decrease of outbreaks of milk-borne disease.

In 1938 the United States Public Health Service¹⁵ began the collection of data on outbreaks conveyed through foods other than milk and milk products. In that year there were 70 food-borne outbreaks, with 2247 cases and 25 deaths. In one of them, which occurred in Fitchburg, Massachusetts, there were 157 cases of gastroenteritis among 175 persons who ate Greek pastry at a memorial church meeting. In 1939, there were 148 food-borne outbreaks, with 3782 cases and 12 deaths.¹⁶ The foods chiefly responsible, in order of number of outbreaks, were pies and pastries (32 outbreaks), pork and pork products (21), meat and meat products (11), home-canned vegetables, fruits, fish and meat (10), salads (8), sandwiches (7) fowl (7), crab meat (5) and sauces and gravies (5). The commonest diseases as classified by Fuchs⁷ were food poisoning (88 outbreaks), gastroenteritis, including diarrhea (88), paratyphoid fever (37), botulism (9), scarlet fever (5) and dysentery (2).

From 1938 to 1941,¹⁵⁻¹⁸ there were 656 food-borne outbreaks, with 17,529 cases and 120 deaths. The commonest diseases in order of numerical importance (Table 2) were food poisoning other

TABLE 2. *Disease Outbreaks Conveyed through Foods Other than Milk and Milk Products in the United States, 1938-1941.*

DISEASE	No. OF OUTBREAKS	No. OF CASES	No. OF DEATHS
Botulism	25	64	33
Chemical poisoning	7	87	14
Dysentery	16	1038	3
Food poisoning:			
Staphylococcal	208	4865	6
Other	229	6096	7
Gastroenteritis	75	3845	4
Paratyphoid fever (Salmonella infection)	14	475	1
Streptococcal infection	1	40	0
Trichinosis	30	246	14
Typhoid fever	46	578	37
Miscellaneous	5	195	1
Totals	656	17529	120

than staphylococcal, staphylococcal food poisoning, gastroenteritis, dysentery, typhoid fever, paratyphoid fever and other *Salmonella* infections, trichinosis, chemical poisoning, botulism, and streptococcal infection.

The responsible vehicles as recorded by Fuchs¹⁵⁻¹⁸ (Table 3), were correlated with the type of disease. Canned foods were the sole vehicle for botulism. Dysentery was most frequently transmitted by an unrecognized food (perhaps owing to a longer incubation period), salads and soups. Chemical poisoning was conveyed by various foods,

including puddings. Food poisoning other than staphylococcal, staphylococcal food poisoning and gastroenteritis were transmitted by nearly all types of foods, the most important for the first two being pastries and ham, and for the third pastries

per cent) of 262 in 1941. Of the 823 outbreaks in the entire period, 80 per cent were transmitted by a food vehicle other than milk and only 20 per cent by milk or a milk product. Moreover, in 1938 and 1939 food-borne outbreaks were more numer-

TABLE 3 *Disease Outbreaks Conveyed through Foods in the United States Relation between Type of Food and Disease*

Food	BOTULISM		DYSENTERY		CHIFFONADE POISONING		FOOD POISONING OTHER THAN STAPHYLOCOCCAL		STAPHYLOCOCCAL POISONING		GASTROENTERITIS		PARATYPHOID FEVER		SCARLET FEVER		TRICHINOSIS		TYPHOID FEVER		OTHER	
	O	C	O	C	O	C	O	C	O	C	O	C	O	C	O	C	O	C	O	C	O	C
Canned food																						
Commercial	2	5	-	-	-	-	1	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Home	23	59	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dressing (stuffing)	-	-	-	-	-	-	3	215	2	128	1	9	1	7	-	-	-	-	-	-	-	-
Fish	-	-	-	-	-	-	14	551	2	20	12	568	1	11	-	-	-	-	4	31	-	-
Graves etc	-	-	-	-	-	-	3	66	4	143	4	75	-	-	-	-	-	-	-	-	-	-
Pork products																						
Ham	-	-	-	-	-	-	27	226	46	1273	5	192	-	1	96	1	7	-	-	2	15	-
Other	-	-	-	-	-	-	16	389	9	38	3	108	-	-	-	27	232	4	61	-	-	-
Meat other than pork products	-	-	-	-	-	-	22	603	12	522	13	1367	-	-	-	1	5	1	17	-	-	-
Poultry	-	-	-	-	-	-	30	12	8	284	5	92	1	21	-	-	-	4	77	2	49	-
Pastries	-	-	-	-	-	-	46	360	75	1365	16	311	-	-	-	-	-	-	-	-	-	-
Puddings etc	-	-	-	-	2	73	2	73	1	52	3	33	-	-	-	-	-	-	-	-	-	-
Salads	-	-	3	181	-	-	18	811	9	315	6	121	1	11	-	-	-	2	67	3	63	-
Sandwiches	-	-	-	-	-	-	12	76	10	579	4	116	-	-	-	-	-	1	71	-	-	-
Soup	-	-	1	6	-	-	4	122	1	23	-	-	-	-	-	-	-	14	149	-	-	-
Miscellaneous	-	-	-	-	5	73	11	320	4	177	2	17	-	-	-	-	-	-	-	-	-	-
Unknown	-	-	12	851	1	10	33	690	2	49	12	9	0	4	195	1	27	14	101	-	-	-
Totals	25	64	16	1038	8	156	242	5775	185	4968	86	364	8	364	29	244	45	517	7	129	-	-

O = number of outbreaks C = number of cases

and meats other than ham and pork. Paratyphoid fever was carried chiefly by stuffing, fish, poultry and salads, scarlet fever by ham, trichinosis by pork, and typhoid fever by pork products, fish, poultry and salads. Pastry was responsible for more outbreaks of most diseases than any other known single food; it was usually filled with cream or custard.

The annual increase in the number of recorded outbreaks is due in part to better reporting. As yet, there are several states that are not reporting food-borne disease. Three states reported over half of the outbreaks in 1939. This difference in reporting is not a true indication of the actual prevalence of food-borne disease. The states that reported large numbers of outbreaks are equipped with active epidemiologic units and have made more complete studies.

An analysis of the prevalence of outbreaks for 1938 to 1941, inclusive, reveals that food is a far more prolific source of food-borne disease than is milk alone. Of 112 outbreaks in 1938, 70 (61 per cent) were spread by a food other than milk, and in 1939 the number was 148 (78 per cent) of 189 outbreaks. Food other than milk was the vehicle in 218 (84 per cent) of 260 in 1940, and 223 (85

per cent) of 262 in 1941. Of the 823 outbreaks in the entire period, 80 per cent were transmitted by a food vehicle other than milk and only 20 per cent by milk or a milk product. Moreover, in 1938 and 1939 food-borne outbreaks were more numer-

ous than water-borne, Fuchs⁷ recording 91 water-borne outbreaks as compared with 301 where the vehicle was food. A further example of the prevalence of food-borne disease is furnished by data from Worcester, Massachusetts. During 1941, 2 outbreaks were recorded. In 1942, when the Worcester Department of Public Health became especially interested in food-borne disease, there were 11 outbreaks, with 230 cases. Undoubtedly there were other outbreaks that were not brought to the attention of the department. Assuming that the prevalence of food-borne disease is the same in the remainder of Massachusetts and in the United States as it is in Worcester, there should have been reported a total of 247 outbreaks in Massachusetts and over 7000 in the United States. In short, food borne disease is more prevalent than is indicated by the reports of health departments.

FOOD INFECTION

Amebiasis

Since the Chicago outbreak¹⁰ in 1933, amebic dysentery has ceased to be regarded as a tropical disease. There is no doubt that this disease is more prevalent in the tropics than elsewhere, as

shown by its spread through food handlers among the Americans stationed at Aruba in the Caribbean. Schoenleber²⁰ found that the stools of over 25 per cent of the men were positive for amebas after several years of residence. An amebic colitis rate of 36.8 per 1000 per annum was reached. Examination of the stools of food handlers revealed that 33 per cent were carriers. Active control of food handlers resulted in a 50 per cent reduction in the incidence of amebiasis after one year, and 92 per cent after three years. The control of food handlers consisted of the examination of the stools of all new employees; those with amebas in their stools were rejected. Stool examinations were reported every month, and if amebas were found, the person was removed from duty, treated with a course of carbarsone or yatren, and returned to duty when three successive stool examinations were negative. Strict hand-washing and fingernail-cleaning routines were instituted. Examination of Italian prisoners²¹ from Africa by British Army physicians revealed that asymptomatic carriers of *Shigella dysenteriae* and of *Endamoeba histolytica* cysts were potential sources of epidemics among prisoners. Four carriers who had no symptoms and no recurrence for three to fifteen months were carriers of the former, and two of these were also carriers of the latter.

The Chicago outbreak was the first recognized epidemic of the disease in a civilian population in the United States. At first, the investigators believed that it was due to a high carrier rate among the food handlers of the hotels that were the focus of the epidemic.²² Of 364 food handlers examined in September, 1933, 11 were carriers and 15 were active cases. In October, the food handlers and other employees were re-examined. There were newly positive stools in 60 of the food handlers and in 100 of 498 other employees. Twenty-three additional carriers were found by culturing the stools. Because the 1400 patients in the two hotels subsequently returned to their homes, cases were scattered among the residents of forty-three states, three Canadian provinces and the Territory of Hawaii. On their return home, forty per cent of the patients were subjected to operation because the illness was mistaken for appendicitis. The mortality rate among all the cases was only 7 per cent. The *Journal of the American Medical Association*²³ published a special review on amebic dysentery as a guide to physicians who were treating patients who had visited the Chicago hotels.

Subsequent investigation²⁴ revealed that the epidemic was due to infected drinking water. Through faulty plumbing, fresh sewage from an-

other hotel was introduced directly into the drinking water supply of the two hotels. Chlorination was sufficient to kill the pathogenic bacteria, but was not effective against the amebas, which are more resistant to chlorine. In 1935, Hardy and Spector²⁵ reported another Chicago water-borne outbreak of amebic dysentery among firemen and spectators who drank from a heavily contaminated auxiliary water supply used to extinguish an extensive stockyard fire.

McCoy,²⁶ of the United States Public Health Service states, "In the World War, bacillary and amebic infections occurred side by side in some military units, and occasionally in the same person." The sources of infection were a human carrier or case, a contaminated water supply, uncooked vegetables from soil fertilized with human excreta, and flies. The same author²⁷ subsequently wrote that the clinical cases originating in Chicago did not lead to any considerable spread of the disease in communities to which the patients went. He pointed out that control of amebic dysentery by routine examinations of stools of food handlers for the detection of carriers and their subsequent exclusion from food handling did not appear to be practicable on a large scale. Nor is there, he states, any need for the isolation of a case; and, when sanitary disposal of feces is practiced, there is no need for special precautions in the care of stools. The control of amebic dysentery, according to McCoy, depends on the diagnosis and reporting of all cases of dysentery, the recognition of the etiologic agent through adequate laboratory procedures, the education of food handlers in personal hygiene, particularly in washing their hands after visiting the toilet, the examination of stools of food handlers during outbreaks of the disease and the provision of safe water supplies by the elimination of faulty plumbing, cross connections and similar sources of pollution.

Spector²⁸ reviewed the literature on the results of surveys of infestations with *histolytica* and described the epidemic prevalence of a small variant of the organism from December, 1933, to summer of 1934 in Chicago. Tonney et al.²⁹ discuss various laboratory methods used for the diagnosis of amebiasis in the Chicago outbreak and the differential diagnosis of other intestinal protozoa.

Most of the recent surveys indicate that Craig's initial estimate that 5 to 10 per cent of the population are infected with *E. histolytica* is still correct. Tsuchiya and Jean³⁰ report 2 to 5 per cent of first-year medical and dental students in Missouri as positive. Dienst³¹ reports 4 per cent of 245 students at the University of Georgia School of

Medicine as positive, and Faust³² found 13 cases positive for *E. histolytica* in the post-mortem examination of 202 cases of accidental death in New Orleans.

The treatment of amebic dysentery was discussed at the Cornell University Medical College Conference on Therapy.³³ Two types of medication were said to be effective; the arsenicals, such as carbarsone and hydroxyguinoline (yatren), and alkaloids, such as emetine hydrochloride.

As a consequence of the war, amebic dysentery is likely to awaken new interest in the medical profession. Since it is endemic in temperate zones and is more prevalent, at times even epidemic, in the tropics and subtropics, soldiers may become infected and bring home the disease after demobilization. During World War I, 926 cases of amebic dysentery were reported.³ Since our troops are more numerous in the present conflict and are in areas where the disease is prevalent, a higher incidence is to be expected.

Trichinosis

Augustine,³⁴ who studied the problem of trichinosis in New England, points out that until drastic changes are made in the methods of garbage disposal, the only effective means of control must remain with the housekeeper; this means that all pork must be thoroughly cooked before it is eaten. Perkins³⁵ discusses the prevalence of this disease in New York and points out that the feeding of raw garbage to hogs is the prime factor responsible for the spread of the disease. He cites two recent outbreaks of trichinosis: the first, involving 20 cases among German-Jewish refugees; and the second, 11 cases from food eaten at a church supper.

Wright³⁶ made a study of the various methods of cooking garbage prior to feeding it to hogs as a means of preventing trichinosis. He discusses the methods used throughout the western and southern portions of the United States, describing the equipment, costs and operation. The costs for fuel and labor varied from 40 cents in the South to \$3.50 on the West Coast. This author believes that cooking garbage is a feasible method for the prevention of trichinosis in hogs and thereby in human beings.

An editorial³⁷ covering progress in the control of trichinosis states that its prevalence in man is proportionate to that in hogs. In Boston, 28 per cent of the adults and 18 per cent of the hogs are infested. In San Francisco, the rates in 1938 were 24 and 15 per cent, respectively, but following the institution of rodent control in the piggeries, the rate of infestation in hogs dropped to 4 per cent in 1941. In the Hawaiian Islands, 14 per cent of wild hogs were trichinosis, but when they were

kept in concrete or wooden pens and fed cooked garbage, the rate dropped to 0.3 per cent. In Canada, all garbage-feeding hog ranches are required to be licensed and inspected, and all garbage is cooked prior to feeding. Inspection includes rodent control. Swine trichinosis has been reduced to 0.2 per cent.

Witebsky et al.³⁸ discuss the serodiagnosis of this disease by means of the complement-fixation reaction. The test is sensitive and specific. It can be carried out as a quantitative procedure, and the increase and decrease of the antibody titer can be observed over a period of time.

Outbreaks of trichinosis are usually limited to families, institutions or other units that are fed from the same kitchens. Four cases of trichinosis occurred in March, 1942, in upper New York State.³⁹ A farmer who purchased a four-month-old pig in the summer of 1941 raised it on cooked food alone. In February, the hog was slaughtered, salted and smoked, and the farmer ate the pork raw in fairly large quantities. On March 3, he became ill and was hospitalized and a diagnosis of trichinosis was made. Three other members of the household became ill with trichinosis, and a dog that had access to the meat developed tenderness of the legs. Two other outbreaks are described by the New York State Department of Health. The first of these involved 7 cases and 2 deaths in a family where a hog fed on kitchen scraps and grain was eaten.⁴⁰ Some of the meat was eaten fresh, but more than half of it had been salted and cooked by frying. The second epidemic involved 19 cases and 1 death in four households.⁴⁰ The pork responsible for this epidemic was obtained from a garbage-fed pig that had been made into sausages. Several lots of these were given to friends, thereby causing 7 cases among three other households.

Spink and Augustine⁴¹ studied 65 cases in Boston and found that in 46 per cent no relation between the disease and the food eaten was established. They studied the trichinosis infestation of rats; of 193 trapped in large piggeries about twenty miles from Boston, only 2 were infested; of 17 captured in a meat packing house, 5 (30 per cent) were infested; of seventy rats caught in the Boston market or waterfront district, 9 (13 per cent) were trichinosis. According to this study, rats do not play an important role in transmitting trichinae to hogs that eat them. Morrison⁴² studied trichinosis among patients at the Beth Israel Hospital in Boston. In the seven years preceding 1935, there were 7 cases, in 4 of which the patients admitted having eaten pork. Diagnosis was established by biopsy and by the presence of eosinophilia.

In Maine, Drake et al.⁴³ studied an outbreak

of 56 cases among 71 persons who ate sausage made by an Italian from the meat of a garbage-fed hog. Ferenbaugh and his associates⁴⁴ reported on an outbreak of 64 cases in a CCC camp at Waterbury, Vermont. Roast pork loin, the center of which was undercooked, was traced as the source. The average incubation period was twelve days. Five biopsies revealed 8 to 800 larvae per gram of muscle.

About one third to one half of a company of soldiers developed trichinosis at Camp Edwards in June, 1942, after eating pork products almost daily. The onset was sudden, and the most frequent symptoms were malaise, weakness, dizziness, frontal headaches, aching of muscles of the back and extremities, swelling about the eyes and gastrointestinal disturbances. Marble, Skoog and Bucholz⁴⁵ were impressed by the persistent fever, marked prostration, severe headache, muscle pains, swollen eyelids, reddened eyes and tachycardia of the 13 soldiers that were hospitalized. These authors emphasize the fact that inspection of meat does not assure safety from trichinae, and that the only control available to the military personnel is thorough cooking of all pork products.

Typhoid Fever

The typing of *Eberthella typhi* by the method of Craigie and Yen⁴⁶⁻⁴⁸ has assisted epidemiologists in tracing the source of outbreaks of typhoid fever. Lazarus⁴⁹ reports on the typing of 465 cultures from eleven western states. At the present time, unfortunately, this procedure is carried out in only a few laboratories. However, if health officers adopt the typing of strains of *E. typhi*, they can usually ascertain the actual source of epidemics. Eliot and Cameron⁵⁰ found the *Vi* agglutination test an aid in epidemiologic investigations of rural typhoid fever.

The isolation of *E. typhi* from stools with different types of mediums was reported by Mayfield and Gober.⁵¹ These workers made 724 isolations, using three mediums as follows: 535 (74 per cent) with lithium chloride Endo agar, 591 (82 per cent) with desoxycholate citrate agar and 601 (83 per cent) with bismuth sulfite agar. They recommend that all three mediums be used routinely, since not all strains were isolated with any one medium.

The New Zealand Department of Health⁵² describes a milk-borne outbreak of typhoid fever occurring from February to April, 1942, at Otahuhu, near Auckland. There were 26 cases and 4 deaths, and a carrier on a milk farm was responsible. Removal of the carrier as a milk handler and pasteurization of the milk stopped the outbreak. Duff and Hardison⁵³ describe an unusual meat-borne typhoid-fever outbreak in Cumberland County,

Tennessee. Seven cases resulted from souse prepared by a chronic typhoid carrier. *E. typhi* was isolated from the souse three months after its preparation.

Bowman⁵⁴ describes 3 outbreaks of typhoid fever from December, 1939, to March, 1940, in Manitoba, Canada, apparently due to cheese made from raw milk and sold without aging. There were 9 cases in the first outbreak, 21 in the second, and 64 in the third. Investigation revealed that two workers at the cheese factory were discharging typhoid bacilli in their stools and that neither had a history of typhoid fever. One of these had apparently been infected by the cheese; his stools became negative in four months. The other was a carrier, and typhoid bacilli were grown from his bile. He had started work in November, 1939, about a month before the outbreaks began. The cheese was allowed to dry for eight days and was sent to the wholesaler on the tenth day. The outbreaks were stopped by removing the carrier as a milk handler and by requiring adequate aging of the cheese. As a result of these outbreaks, Ranta and Dolman⁵⁵ studied the survival of typhoid organisms in Cheddar-like cheese. At room temperature, the organisms were detectable for one month; in the refrigerator, survival was prolonged. In one sample, *E. typhi* was recovered seventeen weeks after inoculation. Experiments demonstrated that the typhoid bacillus penetrates cheese by capillary traction.

Bootlegged oysters were responsible for an outbreak of 81 primary and 13 secondary cases of typhoid fever in Louisiana in 1940. Old and Gill⁵⁶ traced the outbreak to a chronic carrier who gathered and subsequently infected the oysters, which were sold in the shell and opened by the purchasers.

In New York, a trailer camp was the focus of a typhoid-fever outbreak in 1938.⁵⁷ There were 18 cases and 3 deaths. The vehicle was water from a well located in fissured limestone and subject to pollution by nearby cesspools and privies.

Morris et al.⁵⁸ report an outbreak of typhoid fever in a group of Negro families in Twiggs County, Georgia, in September, 1940. Two children who died on the twelfth day of "colitis" were the source of the outbreak. The small-colony variety of *E. typhi* was isolated by the authors by employing plating mediums containing utilizable sulfur.

In 1942, Rubenstein⁵⁹ reported the occurrence of hospital infections of an intern and nurse from unrecognized cases of typhoid cholecystitis. He advocated the protection of hospital personnel by routine antityphoid inoculation and advised considering all patients with cholecystitis as potential

typhoid carriers. An editorial in the *Journal*⁶⁰ estimates that there are 1500 typhoid carriers in Massachusetts, of which only about one tenth are known to the Department of Public Health. It points out that more than 3 per cent of persons who contract typhoid fever continue to harbor the organism, usually in the gall bladder, during the remainder of their lives, and urges physicians to make careful inquiry concerning previous typhoid fever in all cases of cholecystitis. Ames and Robins⁶¹ made a study of the age and sex factors in the development of the carrier state among typhoid-fever patients in New York. Patients over thirty years of age became chronic carriers nine times as frequently as did younger patients. The rate of development of the carrier state at all ages was 2 per cent among males and 4 per cent among females. Sixteen per cent of the female typhoid-fever patients between the ages of forty and forty-nine became chronic carriers. By applying a modified life table based on the experience of New York, these authors estimate the carrier prevalence on January 1, 1940, as 42 carriers per 100,000 population, or 2500 carriers in New York, exclusive of New York City. They estimate that by 1980 the carrier prevalence will decrease to about 200. Four hundred and nineteen (17 per cent) of these estimated carriers were under supervision on January 1, 1940.

There are conflicting reports in the literature concerning the efficacy of sulfaguanidine in the treatment of typhoid carriers. Levi and Willen⁶² treated favorably with 0.5 gm. of sulfaguanidine per kilogram of body weight every eight hours for one week a carrier who had had a cholecystectomy prior to the use of the drug. Saphir et al.⁶³ treated unsatisfactorily 4 carriers with sulfaguanidine over a period of two weeks. Cutting and Robson⁶⁴ treated 6 carriers with a variety of drugs and sulfaguanidine, without success. One of these carriers had had a cholecystectomy prior to treatment. Hoagland⁶⁵ treated 2 intestinal carriers, one chronic and one convalescent, successfully by large doses of sulfaguanidine. The drug is probably not efficacious in chronic gall-bladder carriers, since such carriers in Massachusetts⁶⁶ treated with sulfaguanidine continued to discharge the organism in their stools.

(To be continued)

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29231

PRESENTATION OF CASE

First admission. A fifty-four-year-old painter entered the hospital because of dyspnea, ankle edema and "severe laryngitis."

Each spring of the three years prior to admission the patient had had an attack of "laryngitis." At the same time he also noted slight dyspnea on exertion, slight ankle edema and abdominal swelling. Thirteen months prior to admission his physician treated him with digitalis. One month later he entered another Boston hospital, where he gave a long history of alcoholism, often drinking more than a pint of whisky a day. After an abdominal paracentesis he felt much better. He was found to have a positive blood Hinton test, the spinal fluid had a protein of 37 mg. per 100 cc. and showed a positive Hinton test, a negative Wassermann test and a midzone rise in the gold-sol curve. He was started on antisyphilitic therapy and was told to eliminate alcohol. Accordingly he limited himself to four glasses of beer a day. After discharge he was followed in the syphilis clinic, where he received alternate courses of Mapharsen and bismuth subsalicylate. Spinal fluid obtained six months prior to admission showed a positive Hinton test but a negative gold-sol curve. During the next five months dyspnea on exertion became so severe that the patient was unable to climb two flights of stairs without resting several times. Four weeks prior to admission he developed marked hoarseness and a "cold" characterized by coryza and cough productive of half a cupful of yellowish sputum a day. During the next two weeks he noticed bits of red blood in his sputum. Simultaneously he began to have frequent epistaxes, although his blood pressure was said to have been 150 systolic, 60 diastolic. The cough gradually improved but his voice remained weak and hoarse. Topical sprays did not relieve the difficulty. One week before admission dyspnea became marked, orthopnea developed, and the ankles and lower legs became quite swollen. At no time did he have

*On leave of absence.

precordial pain, palpitation, jaundice, hematemesis, or bloody, tarry or acholic stools.

The family history was noncontributory. At the age of twenty he had had typhoid fever, but this cleared without apparent sequelae. He had a questionable penile sore thirty-one years before entry.

Physical examination disclosed an acutely ill, dyspneic man whose face was mottled and purplish red and whose lips and nailbeds were moderately cyanotic. The neck veins were moderately distended. The pupils were equal and small and reacted to light. Small hemorrhages were seen in the inferior portion of the right fundus. The tongue was red, and smooth at the edges. The pharynx was markedly congested. Expansion of the chest was poor on the right. Over the lower two thirds of the right chest posteriorly and in the right axilla there were dullness to flatness on percussion and diminished to absent tactile fremitus and breath sounds. Grocco's triangle could be outlined readily by percussion. Many moist rales were audible at the left base and in the left axilla. The left border of the heart was percussed 3 cm. beyond the left midclavicular line. The sounds were of fair quality. The aortic second sound was greater than the pulmonic. A harsh systolic murmur was audible at the base of the heart, best heard in the pulmonic area. No diastolic murmurs were heard, and there was no widening of the supracardiac dullness. The abdomen was moderately distended. Slight tympany was percussed in the midportion. Slight shifting dullness in the flank and a fluid wave were demonstrated. The liver edge was felt five fingerbreadths below the right costal margin, and the spleen three fingerbreadths below the left costal margin. The prostate was twice normal size, smooth and nontender. There was marked pitting edema of the legs to the knees.

The blood pressure was 210 systolic, 65 diastolic. The temperature was 101.2°F., the pulse 91, and the respirations 30.

Examination of the blood revealed a red-cell count of 5,830,000, with a hemoglobin of 11.5 gm., and a white-cell count of 5750, with 72 per cent neutrophils, 14 per cent lymphocytes, 11 per cent monocytes and 3 per cent eosinophils. The urine was acid and had a specific gravity of 1.008; the sediment contained 30 to 35 white cells per high-power field. A blood Hinton test was positive, and a Wassermann test negative. The stool was watery, brown and guaiac negative. The serum protein was 8.2 gm., the albumin 4.8 gm., the globulin 3.4 gm. and the nonprotein nitrogen 24 mg. per 100 cc. The prothrombin time was 28 seconds (normal, 22 seconds). A bromsulfalein

test showed 30 per cent retention of the dye in the serum. A throat culture was negative for beta-hemolytic streptococci. An electrocardiogram showed normal sinus rhythm, with a rate of 75. The PR interval was 0.14 second; the ST segment was depressed in Leads 1, 2 and 4; the T wave was diphasic in Leads 1 and 2 and low in Leads 3 and 4.

An x-ray film of the chest was unsatisfactory. The cardiac shadow was within the upper limits of normal. The right leaf of the diaphragm and the costophrenic angles were obscured by fluid. The pulmonary and hilar markings were somewhat prominent. The lung fields were clear.

Soon after admission 1150 cc. of yellowish-red cloudy fluid, having a specific gravity of 1.008, was removed from the right pleural space. The vital capacity was 2.4 liters. After digitalization and the use of diuretics the patient seemed markedly improved but his temperature continued to range between 99.4 and 101.2°F. each day, and the hoarseness continued. On the ninth hospital day he coughed up a small amount of blood and his voice was practically gone. Examination of the larynx after topical cocaine anesthesia disclosed that the right vocal cord was nearly immobile and that the left moved poorly. Both were coated with dried mucus. The mucous membrane of the entire oral cavity was markedly congested.

X-ray examination of the pharynx and hypopharynx showed no evidence of disease, but there was some delay in emptying. An x-ray film of the chest nine days after admission showed that the fluid in the right pleural cavity had increased since the initial examination.

Another chest tap on the twelfth hospital day recovered 175 cc. of dark-red fluid, which contained 200,000 red cells per cubic millimeter. No tumor cells were seen.

Films after thoracentesis revealed the presence of encapsulated fluid in the posterolateral portion of the right lower chest. In addition there was a small amount of free fluid. There was evidence of a fracture of at least several weeks' duration, with callus formation, involving the right eighth rib in the anterior axillary line. There was also an additional fracture of the tenth rib in a similar position, with only a small amount of callus formation about the rib.

The patient gradually improved on supportive treatment, although the hoarseness remained unchanged, and was discharged on the twenty-sixth hospital day.

Final admission (two months later). The patient re-entered the hospital because of sudden pain in the right chest.

Since his last admission the hoarseness had become worse, and exertional dyspnea and cough, occasionally productive of small amounts of blood, continued but did not incapacitate the patient. An x-ray film of the chest, in the Out Patient Department, one month prior to admission, showed persistence of considerable encapsulated fluid in the right posterior chest. Callus was seen about both of the rib fractures. During the month prior to admission the patient had a rather marked swelling of both lower legs, and an ulcer developed over the right medial malleolus. Five days prior to admission he experienced a sudden, severe, sharp pain in the right chest. This persisted to the time of admission and was aggravated by deep breathing. The patient felt feverish and had several shaking chills. Breathing became progressively more difficult and wheezing in character. Two days before entry he began to cough up greenish sputum faintly tinged with blood.

Physical examination disclosed a large, well-developed, well-nourished, red-faced, slightly cyanotic man who coughed frequently, bringing up small amounts of rusty sputum. He breathed with a slight expiratory grunt, and his voice was hoarse and weak. By percussion the heart was enlarged to the left anterior axillary line. The scleras were moderately icteric. The right pupil was irregular in shape and reacted poorly to light. There were flatness and diminished to absent breath sounds over the lower right chest posteriorly. The right upper lung field posteriorly and the entire right lung anteriorly were dull to percussion. Breath sounds were reduced and moist rales were audible in this area. The left lung was entirely clear. The abdomen was moderately protuberant, and the non-tender edge of the liver was felt three finger-breadths below the right costal margin. The tip of the spleen was felt below the left costal margin. Shifting dullness was present in the flanks. There was a 3-cm. oval varicose ulcer over the medial malleolus of the right foot. Homans's sign was negative bilaterally.

The blood pressure was 170 systolic, 85 diastolic. The temperature was 103°F., the pulse 110, and the respirations 35.

The red-cell count was 3,380,000, with a hemoglobin of 10.5 gm., and the white-cell count 10,000, with 96 per cent neutrophils. The urine was acid, had a specific gravity of 1.014 and gave a ++ test for albumin; the sediment contained an occasional white cell and red cell per high-power field.

A roentgenogram of the chest showed diffuse hazy density overlying the entire right lower lung field. There was a localized area of increased density at the base of the right upper lung field.

On the second hospital day, coarse and medium moist rales became prominent on both sides of the chest. The white-cell count was 13,000. The patient was given Mercupurin and sulfadiazine without any apparent response. Cyanosis and jaundice deepened, and incontinence of urine developed. He died approximately forty hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. REED HARWOOD: Perhaps we should look at the x-ray films first.

DR. LAURENCE L. ROBBINS: These are the films taken at the time of the first admission. They show some hazy density in the right lower lung field, and slight increase in the vascular markings and the hilar shadows. I think this spot film was taken at that time to demonstrate what I take to be an encapsulated area of fluid.

The fractures that were described are seen here. There is relatively little callus formation. From what I can see I think they could be fractures that were probably not due to metastatic lesions, but I cannot be sure because they were not taken with rib technic. This one in the tenth rib appears to be an ordinary traumatic fracture that is healing normally. The margins of the fracture are somewhat irregular.

DR. HARWOOD: Could the fracture have any relation to the encapsulated fluid higher up?

DR. ROBBINS: Fractures cause hemorrhage in the pleural cavity but I am not at all sure that that is what happened in this instance.

These are the films that were taken, I presume, a month before the second admission, and here again we have evidence of fluid, which is probably free, with a suggestion of an encapsulated area in this region. In the film taken on the second admission, there is a definite area of density in the right upper lobe, with increase in the amount of fluid. I am suspicious of something in the root of the right hilus.

DR. HARWOOD: Is there anything suspicious at the hilus in the film taken at the first admission?

DR. ROBBINS: No. The only suspicious hilar shadow is seen on the last film taken.

DR. HARWOOD: Do you see any evidence of aneurysm or aortitis?

DR. ROBBINS: No.

DR. HARWOOD: Do you see any evidence of tumor?

DR. ROBBINS: There are only two things that suggest tumor: the presence of fluid and the fractures. As I said, I am not at all certain that the fractures represent areas of metastasis, but that is a possibility.

DR. BENJAMIN CASTLEMAN: I have just noticed a statement in the Out Patient Department record that should have been in the abstract of the history. The record reads, "The patient states that in January [which was one month before the first admission] he fell down an elevator shaft but does not know whether he had hemoptysis."

DR. HARWOOD: There was adequate trauma to account for the fractured ribs.

This patient had numerous conditions, some of which are perhaps not related to his final illness. I plan to take them up in the reverse order of their importance.

In the first place he had syphilis. From the spinal-fluid findings I believe he had syphilis of the central nervous system. The x-ray films show no aneurysm or widening of the supracardiac shadow, so that I think one can say he did not have clinical evidence of syphilitic aortitis or aortic regurgitation. Syphilis of the liver is a rare disease, as is syphilis of the lung. The treatment that he received probably prevented the development of active syphilitic lesions that would be responsible for the final illness.

Secondly, the patient had evidence of cirrhosis of the liver. This consisted of an alcoholic history, an enlarged liver, an enlarged spleen, ascites and a reduced liver-function test. The patient may have had cancer of the liver. There is no evidence for it, but I cannot exclude it. I simply mention it as a possibility.

Then he had heart disease, the evidence for which, in my opinion, comprises dyspnea, edema, cyanosis, rales at the bases and perhaps also pleural effusion. He improved on digitalis and diuretics. The interpretation of the electrocardiogram depends on whether or not he had had digitalis at the time it was taken. The tracing is consistent with digitalis effect, and the record states that he was digitalized in the hospital. If the electrocardiogram was taken before digitalization, it might be evidence of an old posterior infarction. I am going to say that the patient had hypertensive heart disease with congestive failure.

Other possibilities come to mind only to be excluded. For instance, I see no evidence for endocarditis or cor pulmonale.

In regard to the rib fracture, one must conclude from the revised record that the patient had had an injury and had fractured two ribs, and it is more than possible that part of the disease in the right lower chest was due to the resulting effusion, although I cannot be certain about that. He had two other reasons for effusion in the right chest—congestive failure and, I believe, cirrhosis of the liver, in which pleural effusion is not at all uncommon.

Then we come to the consideration of the respiratory tract. The onset of the final illness probably dates from the time when he caught cold. He had coryza, cough, hoarseness and fever, and the x-ray films show no evidence of parenchymal involvement of the lungs. In the early part of the illness I should have suspected a pulmonary lesion from the fact that he coughed up such large amounts of sputum and blood, but in the absence of x-ray evidence of parenchymal involvement I think one must say that he had a severe infection of the upper part of the respiratory tract. We know that he had inflammation of the pharynx and larynx, and probably of the trachea and the larger bronchial tubes.

Is there an additional note about the bacteriology?

DR. CASTLEMAN: No. They were apparently interested only in ruling out *Streptococcus haemolyticus*.

DR. HARWOOD: It is important to know what the organism was in this case. The respiratory infection did not follow the course of an ordinary cold. In the course of a few weeks one would expect that he would stop coughing and that his voice would clear, but he continued to run a fever and remained hoarse up to the end. Seven days before death he had a sudden onset of pain in the chest, followed by fever, chills, cyanosis and jaundice, and this train of events suggests the possibility of pulmonary infarction. Another possibility is that he had pneumonia as a complication of the severe upper respiratory infection. If infarction, what was the source of the embolus? Was it from a thrombosis in the leg? He had an ulcer on the malleolus and had had, at least at one time, some swelling in the leg, which may have been evidence of thrombophlebitis. However, Homans's sign was negative and I cannot say surely that that was the source of the embolus. This chronic and severe infection in the upper respiratory tract was enough to cause bleeding from the mucous membrane. The bacteria may well have invaded the wall of the trachea or larynx and produced a septic thrombophlebitis in a vein in that region. An embolus from that source could have produced infarction to the right upper lung. My diagnosis is septic infarction of the right upper lung, hypertensive heart disease and congestive failure, cirrhosis of the liver and syphilis of the central nervous system.

DR. JACOB LERMAN: How does Dr. Harwood explain the paralysis of the cord?

DR. HARWOOD: I believe the paralysis was simply edema and congestion from chronic infection.

DR. CASTLEMAN: Did you have anything else in mind, Dr. Lerman?

DR. LERMAN: I was thinking of a patient that I discussed some time ago who had deficiency disease producing diffuse atrophy in the region of the larynx with paralysis.

DR. CHESTER M. JONES: For the sake of the record it may be wise to amend one of Dr. Harwood's statements. Syphilis of the liver is rare in this hospital, but in many places it is relatively frequent. I am sure that it is not rare.

CLINICAL DIAGNOSES

Latent syphilis.
Lobar pneumonia.
Laryngitis (? syphilitic or tuberculous).
Hydrothorax, right.
Cirrhosis of liver (? alcoholic).
Fracture of ribs.
Thrombophlebitis and varicose ulcer, right leg.

DR. HARWOOD'S DIAGNOSES

Septic infarction of right upper lung.
Hypertensive heart disease.
Congestive failure.
Cirrhosis of liver.
Syphilis of central nervous system.

ANATOMICAL DIAGNOSES

Lobar pneumonia, right lung.
Empyema, encapsulated.
Cardiac hypertrophy.
Cirrhosis of liver, alcoholic.
Splenomegaly.
Syphilis of central nervous system?
Chronic laryngitis.
Traumatic fractures of eighth and tenth ribs.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this man had a slightly enlarged heart, weighing 390 gm. There was no disease of the aortic valve, and I am still at a loss to explain the elevated pulse pressure. There was no dilatation of the ascending aorta and no evidence of syphilitic aortitis, grossly or microscopically. The right pleural cavity was almost completely obliterated by numerous old adhesions, and in the posterolateral aspect of the lower portion there was an encapsulated empyema containing about 300 cc. of dirty, greenish-gray, bloody, fibrinopurulent fluid. The wall of the cavity measured 5 to 6 mm. in thickness, which is evidence that the empyema was present at the time of the first admission. The whole right lung was completely consolidated and on section presented the uniform reddish-gray granular appearance characteristic of pneumococcal lobar pneumonia. The left pleural cavity was free from fluid and adhesions. There was no embolism or infarction in the lung.

The liver was moderately enlarged, weighing 200 gm., and had a diffuse, almost regular granularity such as one sees associated with the alcoholic type of cirrhosis. Microscopic examination confirmed this impression, large areas of fatty vacuolization and liver cells with characteristic acidophilic hyaline granular network being seen. The spleen was enlarged, weighing 600 gm. There was a small amount of ascitic fluid.

The vocal cords were edematous and granular, and microscopically there was a marked chronic inflammatory process, with lymphocytic and plasma-cell infiltration. It certainly was not a gumma. The laryngologist might call this a chronic catarrhal laryngitis.

The only evidence of syphilis was a granularity of the ependyma in the floor of the fourth ventricle, a finding usually associated with syphilis of the central nervous system.

Dr. WILLIAM BECKMAN: Five days is a short time to develop encapsulated empyema. If we date the terminal episode from the cold, it was five days from the time of the second admission.

Dr. CASTLEMAN: I believe that the patient had the empyema at the first admission, because it was seen on the x-ray film then, and also because the cavity wall was so thick at autopsy. The cause of this empyema is still in doubt. It may well have been secondary to the rib fractures or perhaps to pneumonia in the lower lobe, which could not be seen on the film because of the overlying fluid.

Dr. ROBBINS: There was no free fluid in the right pleural cavity at autopsy?

Dr. CASTLEMAN: No.

CASE 29232

PRESENTATION OF CASE

A sixty-two-year-old woman entered the hospital complaining of abdominal pain.

The patient had been in perfectly good health for about six months preceding the onset of the present illness. Five or six months before entry, during the early hours of the morning, the patient had an attack of lower abdominal cramps. She attributed this to beans eaten the preceding evening. The attack was followed by exhaustion, but there was no change in the bowel habits, and no residual pain or soreness, and she ignored the incident. About four months prior to admission a similar attack occurred, and again three weeks after that. All these attacks were characterized by rumblings and pain of varying degree definitely increasing with each attack. The cramps were always in the lower abdomen, below the umbilicus, with no radiation or steady pain. Occasionally the attacks were associated with the vomiting of "bitter bile," but the vomiting was rarely pro-

longed. The attacks occurred at night or early morning and always on a Sunday. They were followed by exhaustion for a day or so, and after the first two the patient thought the stools were darker, although they were never frankly black or bloody. After the third attack she called her physician, who gave her some "pills." During the fourth attack he saw her and gave her a hypodermic injection; at that time he advised x-ray study. Films were taken about three weeks before admission and she was then recommended to this hospital. The last attack occurred two weeks prior to admission and was accompanied by even more pain than any of the others. During this period she had lost approximately 6 pounds.

Twenty-eight years prior to admission, following her third pregnancy, the patient stated that she was unwell for four years. During the pregnancy her hands and feet became swollen and she was said to have had kidney trouble. She had had pleurisy following the delivery, and was told that she had anemia and a "spot on her lung." She recovered from this without any particular treatment, and four years later she again became pregnant, without complications. She was well until three years prior to admission, when she felt tired and run down; her doctor told her that she had anemia, not pernicious anemia, and treated her with liver injections for some weeks and then with liver and iron pills. She recovered and stopped taking the pills. One year prior to admission she had a similar episode, again successfully treated with liver and iron. She had taken no liver or iron for eight or nine months prior to entry.

Her family and marital histories were not remarkable.

Physical examination showed a well-developed and well-nourished, pale woman in no apparent distress. The tongue was smooth and pale, with reddened atrophic papillae. The heart was not enlarged. The abdomen was protuberant, soft and tympanitic. No fluid wave or shifting dullness was elicited. There were no masses or tenderness.

The blood pressure was 158 systolic, 90 diastolic. The temperature was 99°F., the pulse 80, and the respirations 18.

Examination of the blood showed a hemoglobin of 13.6 gm. and a white-cell count of 6700 with 71 per cent neutrophils. A blood Hinton test was negative. The urine was normal.

Roentgenograms brought in by the patient showed on both the barium-enema film and the six-hour film of the barium meal an area of narrowing, 3 cm. long, in the ascending colon. The sigmoid showed diverticulosis. A chest roentgenogram was negative.

An operation was performed on the eighth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HORACE K. SOWLES: The x-ray films and the story are somewhat contradictory. The recurrent pain and crampy rumbling with nausea are typical of small-bowel, rather than large-bowel obstruction. It is a fairly typical story of small-bowel tumor, but such a tumor is very rare; a gall-stone obstructing the terminal ileum is commoner than tumor. According to the x-ray films, the lesion is not in the small bowel but in the cecum or ascending colon. So in that respect I should say the x-ray films and the history are contradictory.

The x-ray report does not indicate whether it was a smooth-walled or ulcerated obstruction. If smooth walled it might be suggestive of lymphoma or sarcoma rather than carcinoma or tuberculosis. The patient had a "spot on her lung" twenty-eight years before entry, which is probably of no great significance, although the lesion could have been tuberculosis of the cecum. The anemia was not very marked; we are not told what the blood smear showed. Certainly if she had a carcinoma of the cecum, it had not been there for three years, since they are rapidly growing tumors. I think we can assume that the anemia three years before entry was not due to the present illness. Mild anemia within the year might have been associated with the present lesion, but I am going on the basis that this was probably carcinoma rather than tuberculosis and therefore that the three-year-old anemia was not due to this particular lesion. Of course the patient may not have had a carcinoma of the ascending colon; perhaps the radiologist can tell us more about the films.

DR. LAURENCE R. ROBBINS: These films were taken in another hospital. I know nothing about the fluoroscopy of the patient, but here is the area of narrowing, which is quite localized, with rather irregular margins. I should say that much of it is ulcerated, but I cannot be positive of that from these films.

DR. SOWLES: Could the area of narrowing be in the terminal ileum?

DR. ROBBINS: It is quite difficult to be sure, but I should say that the lesion is close to the ileocecal valve. It could be in the ileum.

DR. SOWLES: Of course that would fit in more with the story of pain and cramps than if it were in the cecum or ascending colon. In that case the x-ray films do corroborate the clinical history of small-bowel obstruction. Tumors of the small bowel, such as carcinomas and lymphosarcomas, are extremely rare. I happened at one time to see four within a period of two years, which was very unusual. I looked them up at that time

and found that in a period of twenty-five or thirty years they had had only 25 or 30 cases at the Mayo Clinic.* I think the best bet is malignant tumor, probably carcinoma or lymphosarcoma, of the terminal ileum.

DR. RICHARD H. SWEET: My interpretation of the patient's symptoms was that her intermittent attacks were possibly due to intussusception of the obvious growth, and that her pain was probably small bowel in origin because of proximity to the ileocecal valve. I thought it was carcinoma. I operated on her and performed a right colectomy. The growth was in the ascending colon, and I did the radical type of right colectomy that one would do for carcinoma. The lesion looked grossly like a carcinoma.

CLINICAL DIAGNOSIS

Carcinoma of ascending colon.

DR. SOWLES'S DIAGNOSIS

Carcinoma of terminal ileum.

ANATOMICAL DIAGNOSIS

Tuberculosis of ascending colon and regional lymph nodes.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: When opened, the specimen showed about 5 cm. from the ileocecal valve in the ascending colon, an annular moderately ulcerated lesion measuring 5 by 3 cm. The margins were ragged, and the base was granular. Histologic examination showed tuberculosis. The regional nodes, which were soft but not large, also showed tuberculosis.

DR. ROBBINS: In the films it does not look as if the lesion were that far from the ileocecal valve. But one cannot be sure of the exact location.

DR. SWEET: It looked farther away at operation. It appeared to be in the middle of the ascending colon. The ileum showed thickening and hypertrophy, as if it had been working against an obstruction for a long period.

DR. CASTLEMAN: There was some secondary infection and necrosis along with the tuberculosis. The intestinal lesion had very little caseation, but there was caseation in the regional nodes.

DR. SOWLES: I think the pathological findings explain the small-bowel type of pain. The ileocecal valve was evidently incompetent.

DR. CASTLEMAN: It is quite possible that there had been intussusception, which produced some of the pain, although one usually associates intussusception with tumors, especially those of the polypoid type.

*Rankin, F. W., and Mayo, C., 2d. Carcinoma of small bowel. *Surg. Gynec. & Obst.* 50:939-947, 1930.

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ONE HUNDRED AND SIXTY-SECOND ANNIVERSARY

THE one hundred and sixty-second anniversary of the Massachusetts Medical Society, held at the Hotel Statler, Boston, on May 24, 25 and 26, was extremely well attended in spite of transportation difficulties and the absence of approximately a fourth of the active members of the Society, who are serving with the armed forces. The total registration was 1275, as compared with 1556 at the meeting in 1942.

At the annual meeting of the Council, the most significant action taken was the approval of the recommendation of the Executive Committee that will permit the Society to acquire additional office

space from the Boston Medical Library, with an appropriate increase in the fee for maintenance. At the request of certain fellows of the Society, the Section of Anesthesiology was created. And, finally, the appointment of two important committees was authorized. One will consider the ways and means of establishing a postwar loan fund for the use of commissioned members of the Society on their return to civilian practice, and the other will assist the OPA in matters pertaining to supplementary food rations demanded by the special diets that are necessary for certain patients. The following officers were elected for the year 1943-1944: president, Roger I. Lee, of Boston; president-elect, Elmer S. Bagnall, of Groveland; vice-president, Daniel B. Reardon, of Quincy; secretary, Michael A. Tighe, of Lowell; treasurer, Eliot Hubbard, Jr., of Cambridge; assistant treasurer, Norman A. Welch, of West Roxbury; and orator, Joseph C. Aub, of Boston.

The routine business at the annual meeting of the Society was perfunctory. The secretary, Michael A. Tighe, reported concerning membership, and the president, George Leonard Schadt, gave the customary annual report on the state of the Society. At the close of the meeting, the orator, Edward P. Bagg, delivered the annual oration, "Small Puddles," which was printed in the May 27 issue of the *Journal*.

Mr. James A. Hamilton, of New Haven, Connecticut, president of the American Hospital Association, was the principal speaker at the annual banquet. He discussed the types of medical and hospital care that will prevail in the future and emphasized the need for physicians and others interested in such problems to support wholeheartedly and enthusiastically all plans that are on a voluntary, rather than a compulsory, basis. The Shattuck Lecture was given by George W. Thorn, Hersey Professor of the Theory and Practice of Physic at the Harvard Medical School, his subject being "Physiologic Considerations in the Treatment of Nephritis." Dr. Thorn stressed the importance of providing a normal food and water

intake for patients with nephritis. He pointed out that maintenance of an adequate plasma-protein level by the intravenous administration of a concentrated solution of serum albumin permits direct treatment of intercurrent episodes of azotemia, dehydration or acidosis by parenteral-fluid therapy. He also mentioned the occasional development of an extensive sodium chloride deficit in chronic nephritis and the importance of plasma-chloride measurements as a guide in the treatment of this situation.

The general scientific sessions were well attended. The papers on the first morning covered various aspects of the Cocoanut Grove disaster, and those in the afternoon were chiefly concerned with wartime medicine. The speakers on the second day discussed general topics of interest and value to the practitioner.

The luncheon meetings of the sections, although considerably less well attended than in the past, went off smoothly, and the technical and scientific exhibits were attractively set up in the Ballroom and Foyer, a location that would be difficult to improve. The motion-picture program was so popular that the seating facilities were inadequate, a circumstance that can undoubtedly be corrected in the future.

All who attended the meeting will testify that the Committee on Arrangements deserves the highest commendation for its efforts.

A SIMPLE LABORATORY TEST FOR PRIMARY ATYPICAL PNEUMONIA

SOME of the difficulties in determining the etiology in cases of so-called "virus pneumonia," that is, the primary atypical pneumonias that are not caused by known bacterial agents, were reviewed in the *Journal* last year,¹ and recent contributions in this field were commented on in the June 3 issue of the *Journal*. At best the isolation and identification of a nonbacterial respiratory pathogen is still a problem for highly specialized research workers, and even in their hands requires long and carefully controlled procedures. The

demonstration of a simple clinical laboratory test that may serve to distinguish some of the cases of virus pneumonia is therefore highly welcome. The finding by workers² at the Thorndike Memorial Laboratory, Boston City Hospital, of cold agglutinins in many cases of this disease during the past months may prove to serve as such a test.

The fact that hemolytic anemia develops in certain severe cases of primary atypical pneumonia and the difficulties encountered in typing the blood in such cases, preliminary to transfusion, led to studies that showed that both these hematologic abnormalities are related to the finding of reversible cold hemagglutinins in the serum or plasma of these patients. Further search revealed that most of the patients with the prevalent severe and extensive forms of primary atypical pneumonia exhibited this abnormality to a varying degree, although hemolytic anemia was only rarely encountered. The cold agglutinins appear only after the illness has progressed for a few days, and the titer then increases as the disease advances. The maximum titers are found at, or soon after, the end of the febrile stage of the illness, after which the titer drops.

Cold agglutinins are easily recognized. They may be suspected if there is difficulty in blood grouping or in the finding of compatible blood donors when the serum of the patient is mixed with his own or with any other person's erythrocytes. If citrated or oxalated blood of such a person is placed in a refrigerator, the cells clump and appear to form a clot, but the mass of cells can be broken up readily by shaking and the clumping can be completely abolished by warming the blood to 37° C. The clumping of the cells sometimes occurs at room temperature and is occasionally noted during a red-cell count. The appearance of agglutination in the cold, its persistence in the cold after dilution of the serum or plasma, and its complete abolition by heating to 37° C. serve to distinguish this phenomenon from other forms of hemagglutination. These autohemagglutinins and reversible cold agglutinins are independent of blood

grouping, and persist after the isoagglutinins are removed from the serum by absorption. In actual tests and titrations, serial dilutions of serum or of plasma from oxalated blood are mixed with a 1 per cent saline suspension of washed human Group (IV) erythrocytes or of the patient's own cells, and the tubes are observed after the mixtures have stood in an ice bath for one hour or in the refrigerator overnight. If positive, the tubes are then placed in an incubator or in a water bath at 37° C to see if agglutination is completely abolished.

The phenomenon is not specific for atypical pneumonia and indeed does not occur in many of the cases that are usually classed as virus pneumonias. It is apparently a rare property that has been previously described only in a small number of cases, which mostly include cases of blood dyscrasias and liver diseases, and has also been associated with thrombosis and other peripheral vascular phenomena. The only other infectious disease regularly concerned with the presence of cold agglutinins is trypanosomiasis, in which they have been found both in human cases and in experimentally infected animals.

The occurrence of cold agglutinins in atypical pneumonia is independent of chemotherapy with sulfonamide drugs. What relation, if any, they have to the etiology of the disease has not yet been determined. The finding has now been corroborated in many clinics³ but it has been demonstrated only in a small percentage of cases diagnosed as primary atypical pneumonia, although it has been found quite regularly in the extensive and severe forms. The bacterial pneumonias, and most of the other common infections that have been studied, are not associated with cold agglutinins. This test may therefore serve as a simple means of distinguishing one of the many forms of the virus pneumonias.

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- 2 Peterson O L, Ham T H and Finland M. Cold agglutinins (antehemagglutinins) in primary atypical pneumonias. *Science* 97 167 1943.
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MEDICAL EPONYM

WASSERMANN REACTION

The first descriptive account of this epoch making procedure appeared in the *Deutsche medizinische Wochenschrift* (32: 745, 1906) in an article entitled "Eine serodiagnostische Reaktion bei Syphilis [A Serodiagnostic Reaction in Syphilis]" by A. Wassermann (b 1866), A. Neisser (1855-1916) and C. Bruck (b 1879). A portion of the translation follows:

This method consists in the mixture of inactivated serum from monkeys previously inoculated with syphilitic material with organ extracts, serum and so forth of syphilitic persons and the addition of complement (fresh, normal guinea pig serum), allowing a certain period for the latter to be bound. Thereupon it is determined by means of an inactivated specific hemolytic serum, together with the blood corpuscles, whether the complement that was first added has been completely or partially fixed. If this is the case, the fact is shown by complete or partial failure of the blood cells to disintegrate, that is, by an arrest of hemolysis.

We may, therefore, say that we have succeeded in obtaining a specific serodiagnostic reaction with syphilitic material.

R W B

WAR ACTIVITIES

CIVILIAN DEFENSE

EMERGENCY DISTRIBUTION OF BLOOD PLASMA

A circular (Medical Series No 27) recently issued by the Office of Civilian Defense in Washington reads as follows:

1 The United States Director of Civilian Defense has made arrangements so that the Civil Air Patrol will fly blood plasma supplies into stricken areas in the event of emergencies.

2 In instances where, owing to bombing, fire, tornado and so forth, it becomes necessary to supplement stocks of blood plasma in stricken areas and where other methods of transportation are not available or are inadequate, the regional medical officer should get in touch with the appropriate wing commander of Civil Air Patrol and request emergency air transportation for the plasma. Wing commanders have been authorized to accept such requests only from the regional medical officers.

3 In such event, the wing commander should be given complete details as to where the plasma is to be picked up and delivered. Arrangements should then be made by the regional medical officer to deliver the plasma to and from the airports.

4 These arrangements will apply for all states except those located within the jurisdiction of the Western Defense Command. In those states it is understood the Western Defense Command has sufficient

nontactical airplanes available to furnish such transportation.

5. Appropriate instructions, which will ensure the efficient operation of this transportation facility, will be furnished to state and local chiefs of Emergency Medical Services by their regional medical officers.

6. The current list of wing commanders, Civil Air Patrol, is being furnished to the regional medical officers.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1943

DISEASES	APRIL 1943	APRIL 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	3	1	1
Chicken pox	1135	2053	1286
Diphtheria	8	13	13
Dog bite	963	1073	959
Dysentery, bacillary	3	9	7
German measles	8651	1983	157
Gonorrhea	379	311	368
Measles	7285	5512	4012
Meningitis, meningococcal	140	23	7
Meningitis, other forms	11	8	•
Meningitis, undetermined	2	2	•
Mumps	770	2411	1109
Paratyphoid infections	42	5	5
Pneumonia, lobar	359	338	540
Scarlet fever	2582	1686	1172
Syphilis	301	553	514
Tuberculosis, pulmonary	273	232	268
Tuberculosis, other forms	19	14	30
Typhoid fever	3	1	2
Undulant fever	3	4	3
Whooping cough	604	931	798

*Pfeiffer bacillus meningitis only other form reportable previous to 1941.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Easthampton, 1; Fitchburg, 1; Malden, 1; total, 3.

Anthrax was reported from: Haverhill, 1; total, 1.

Diphtheria was reported from: Arlington, 1; Boston, 2; Brookline, 1; Merrimac, 2; New Bedford, 1; Salem, 1; total, 8.

Dysentery, bacillary, was reported from: Boston, 1; Fort Devens, 1; Waltham, 1; total, 3.

Encephalitis, infectious, was reported from: Andover, 1; Melrose, 1; Weston, 1; Worcester, 1; total, 4.

Lymphocytic choriomeningitis was reported from: Brockton, 1; total, 1.

Meningitis, meningococcal, was reported from: Amherst, 1; Arlington, 1; Ashland, 1; Boston, 38; Bourne, 1; Braintree, 1; Bridgewater, 1; Brockton, 5; Brookline, 1; Cambridge, 10; Chelsea, 1; Dedham, 3; Everett, 2; Fall River, 4; Falmouth, 1; Fitchburg, 1; Haverhill, 1; Hingham, 1; Holyoke, 2; Hopkinton, 1; Marblehead, 1; Marshfield, 1; Medford, 1; Methuen, 2; New Bedford, 1; Newburyport, 1; Northbridge, 1; Norwood, 1; Quincy, 3; Revere, 1; Rockland, 1; Somerset, 1; Somerville, 4; Southborough, 1; Southbridge, 2; Springfield, 2; Stoughton, 2; Sudbury, 1; Sutton, 1; Taunton, 1; Walpole, 1; Waltham, 7; Watertown, 3; Webster, 1; West Bridgewater, 1; Winchester, 1; Woburn, 2; Worcester, 2; Camp Edwards, 8; Fort Banks, 1; Fort Devens, 3; Westover Field, 1; Chelsea Naval Hospital, 3; total, 140.

Meningitis, other forms, was reported from: Boston, 5; Brockton, 1; Cambridge, 2; Greenfield, 1; Pittsfield, 1; Worcester, 1; total, 11.

Meningitis, undetermined, was reported from: Chelsea, 1; Everett, 1; total, 2.

Paratyphoid infections were reported from: Dalton, 1; Danvers, 34; Peabody, 1; Salem, 3; Sandwich, 1; Worcester, 2; total, 42.

Septic sore throat was reported from: Boston, 9; Cambridge, 2; Foxboro, 2; Haverhill, 2; Merrimac, 1; New Bedford, 1; Springfield, 1; Swampscott, 1; Topsfield, 1; Wakefield, 2; Winchester, 2; total, 24.

Tetanus was reported from: Northbridge, 1; total, 1.

Trachoma was reported from: Boston, 2; total, 2.

Typhoid fever was reported from: Chelsea, 1; Dartmouth, 1; Everett, 1; total, 3.

Undulant fever was reported from: Chelsea, 1; North Brookfield, 1; Southbridge, 1; total, 3.

Weil's disease was reported from: Gloucester, 1; total, 1.

Meningococcal meningitis again reached a new high point, with an increase of 10 cases over last month's record number. There was a marked increase in April in the number of paratyphoid infections; 80 per cent of these, however, occurred in one institution. Scarlet fever continued its upward march, surpassing previous records. Measles and German measles attained high levels, the latter reaching a towering figure fifty-five times the seven-year median.

The following diseases, in addition to those mentioned above, exceeded their seven-year medians: anterior poliomyelitis, dog bite, gonorrhea, pulmonary tuberculosis and typhoid fever.

Below the seven-year median were: chicken pox, diphtheria, bacillary dysentery, mumps, lobar pneumonia, syphilis, tuberculosis (other forms) and whooping cough.

BOOK REVIEW.

A Short History of Nautical Medicine. By Captain Louis H. Roddis, Medical Corps, United States Navy. 12°, cloth, 359 pp., with 12 illustrations. New York: Paul B. Hoeber, Incorporated, 1941. \$3.00.

Captain Roddis of the United States Navy has long been interested in medical history, and a series of his papers on nautical medicine, which have appeared from time to time in the *Annals of Medical History*, are now brought together in book form. A companion volume, not yet published, will consist of a series of biographies of the surgeons general of the United States Navy.

The present book takes up nautical medicine from the earliest time, giving excellent descriptions of diseases and disasters in old sailing ships, the history of the beginning of the medical department in the Navy and the general rise of naval hygiene, particular attention being paid to the United States Navy. There is also a chapter on nautical medicine in the merchant marine, as well as one on uniforms and insignia. In the last chapter Captain Roddis lists the various topics that might be considered under the term of research in nautical medicine.

This is an interesting and well-written book. The facts are chosen with care, for the author is an expert historian. His style, however, is somewhat heavy for popular consumption. There is plenty of romance associated with nautical medicine, which somehow has evaded the author. As a factual treatise on the subject, brief though it is, this book is highly recommended. There are interesting illustrations, but the volume lacks an index.

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MEDICAL ASPECTS OF ABSENTEEISM*

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ABSENTEEISM in industry is only partly a medical problem. It is probably safe to say that about half of the absences are due to medical causes. No matter what the cause, absenteeism is a subject for study by persons who have a real understanding of human reactions under stress. Because of their understanding of human nature and their interest in human reactions and behavior, physicians are definitely interested in this present problem and should be able to contribute much toward its solution. No one of the governing factors, including priorities, lack of essential materials and any other obstruction to all-out production, contributes quite so much to slowing up vitally important production as this habit of present-day workers.

In order to present a clear picture of industrial absences from the viewpoint of causation, they may be conveniently divided into three categories: those due to bona fide cases of illness and non-industrial accident, those due to industrial accident and those due to other causes. The third group is the one with which government and industry are most concerned at the moment. The proper remedy applied to this group will in all probability effect the greatest reduction in lost time.

Figures are available that tell how much lost time can be expected normally among the working population from unavoidable causes, so that it is relatively simple to demonstrate how much of the working time is lost unnecessarily. These figures indicate that 8 days are lost each year by men and 12 days by women because of illness and accident of nonindustrial origin. On the basis of three hundred working days per year, these figures transposed into percentages show that men lose a little less than 3 per cent of their working days and that women lose approximately 4 per

cent of theirs from these causes. Less than one day per employee is lost through industrial accidents.

As of December, 1942, there were 52,500,000 workers in the United States. Seventy-one per cent, or 37,275,000, were men and 29 per cent, or 15,225,000, were women. If one applies the male sickness absentee rate of 8 days per year to the total number employed, it is obvious that a minimum of 420,000,000 man days or 3,360,000,000 man hours were lost during 1942 from this cause alone. When the latter figure is doubled so as to include the time lost from all causes, the present amount of lost productive time through absences becomes approximately 7,000,000,000 man hours; without doubt, this is less than the actual loss.

It is universally recognized that a certain amount of absence from work is absolutely necessary. Medicine could not be practiced successfully if we did not make use of rest for our patients—rest at home, rest in bed or simply rest from the mental and physical strain of the daily routine. No one can deny that the doctor has the interest of his patients at heart above any other consideration, and that any absence from work prescribed by him is necessary. We must also realize how important it is to get these patients back to work as soon as is expedient following an illness or an injury. This is desirable not only under present war conditions, when every man hour is required for war production, but at all other times so far as the patient's financial status is concerned.

This point is constantly being proved to patients and physicians in industrial practice. The man or woman who has been ill may have attained full physical recovery, but there is often a lag in the return of mental alertness and the desire to get going again. It is not unusual for these patients to be depressed and in need of a bit of encouragement. Then is the time to suggest their return to work. Getting back on the job is often the exact tonic needed to effect a complete recovery.

*Presented at the Institute on Industrial Health, held under the auspices of the Committee on Industrial Health, Massachusetts Medical Society, in Boston, April 24, 1943.

†Medical director, Houd Rubber Company.

The reason why some doctors do not suggest this earlier return to work is no doubt the belief that in general industrial jobs are fatiguing. Some of them undoubtedly are, but most of them are not. Industrial management is far more considerate than it was in the era when a workday extended from sunrise to sunset the year around, and when the boss thought that it was his prerogative to dictate even the use of an employee's leisure hours. Employers then in some instances tried to get the last ounce of energy out of the workers for the stipend paid them, but those days have gone. The worker now is "master of his soul" during working hours, and during his leisure hours as well. The modern factory manager has no desire to direct his employees' leisure pursuits, nor does he expect them to give more than a fair measure of their time and effort.

Most factory operations have been brought well within the physical capacities of the average worker, and he is not required to wear himself out on the job. Fatigue is not produced by the day's work alone. It is an accumulated state of weariness brought about by continued application to work and play without sufficient periods of rest.

What has all this to do with absenteeism? It has a definite and important bearing on it. The fatigue that the average worker ascribes to his job is, in his opinion, best relieved by frequent absences from his work. These absences taken at the whim of the worker bring about an unusual degree of lost time that cannot be planned for by management, and many thousands of extra employees are necessary to maintain production.

If daily absences were reduced by only a small percentage, thousands of these extra workers could be freed to do other equally important work. The tardy return of people to work after minor illnesses is not the major cause of absenteeism, but it is an important one. There is nothing new or unusual in this as a cause of absence. It has assumed, however, a greater importance, since absentee rates have mounted from a reasonably normal 3 per cent to an all-time high of 8 or 10 per cent. Every man returned to work a day earlier is going to help.

I do not intend to leave the impression that the return of ill or convalescent people to work is urged. I am referring only to the person who has recovered from his physical illness, but who finds it difficult to get into the right state of mind to take up his job again. When the physician has satisfied himself beyond a doubt that his patient has sufficiently recovered to return, he should suggest it as a therapeutic measure. He can thus do his patient a lot of good and at the same time

contribute immeasurably to the war effort. This is sound medical practice as well as economically sound for patients. Long illness attended by loss of income and heavy medical expense has been disastrous for many wage earners.

It is a natural thing to advise a patient who has recovered and is well able to return to work in the middle of the week that he may just as well wait until the following Monday. This advice is no doubt predicated on the belief that it is upsetting to the plant routine to have a man return in the middle of the week, but this is not so under present conditions. When so many workers are absent every day, a man who returns to work any day of the week will be welcomed with pleasure by his employer. Going back to work in the middle of the week has something to recommend it from the patient's standpoint, in that he may ease himself back into the job by working a day or two and may then have a day of rest before he tackles a full week of work. Careful attention to this alone will give the family doctor an opportunity to contribute much to the war effort, by helping to reduce absenteeism. Many doctors get their patients back to work at the earliest moment consistent with sound medical practice, but some do not. The truth of this statement is proved by figures relating to a recent study of about 700 cases in which disability extended over a period of more than a week. Of these workers, 84 per cent returned on Monday, 10 per cent on Tuesday, 4 per cent on Wednesday, 1.25 per cent on Thursday, 0.75 per cent on Friday, and none returned on Saturday.

I have made a check of the public schools in a suburban town to see how their experience compares with present-day factory experience in percentages of absence, and also in relation to the percentage of return following illnesses by days of the week. The public-school records showed the same trend to return on Monday after an illness of a week or more. The conclusion can logically be reached, therefore, that people react in very much the same way regardless of age and that the habits of early environment have a lasting effect on adult behavior.

Certainly it is not coincidence, and there is nothing to explain this sudden return to health on Monday except the reason I have previously given. The conclusion is obvious. Many of these employees could have returned on some previous day. This is a costly procedure and one that it seems can be corrected easily. We are the ones who can do most to correct it. If the conclusion is correct that 50 per cent of lost time is due to illness, then one day cut from the average per employee will

result in a saving of 52,500,000 times 8 man hours, or 420,000,000 man hours per year.

These astronomical figures are hard to visualize, so for the sake of a better understanding of the meaning, the experience of a plant of moderate size that is fairly representative of the whole industrial picture will be described. This plant employs approximately 5000 people, and two of its war products are airplane de-icers and self-sealing gasoline tanks for fighting planes. One day of work lost by its 5000 employees, if saved and applied to the manufacture of de-icers alone, would provide this vital equipment for 230 planes, or if applied to the manufacture of tanks, would equip 205 planes. Two hundred and thirty planes can do a lot of damage to the Axis. Multiply this by the number of plants engaged in the same type of work, and one begins to realize what it means in terms of production.

Up to this point I have purposely discussed absenteeism from the standpoint of illness and the part that the family physician can play in reducing it, but lost time from this cause is only half the story. There are many other reasons why people stay away from work so frequently.

One of the major changes that have taken place in industry, and one that has contributed greatly to increased absenteeism, is the reduction in the number of men employed and a corresponding increase in the employment of women.

The plant previously mentioned employs about 5000 workers, and during a normal period 60 per cent of these were men and 40 per cent women. The rate of daily absence was 3 per cent, and the peak of absence prior to the war was reached during the influenza epidemic of January, 1911, when it went to 7 per cent. Since the war began the Army and Navy have drawn heavily from the manpower of this plant, so that sex distribution has changed to 34 per cent men and 66 per cent women. With this change there has been an increase in absence from 3 per cent to 8.5 per cent, an all-time high. Can this increase be chargeable to the increased employment of women? Most of it can!

It has already been said that women lose 50 per cent more time than men because of illness, and therefore four days of absence is added to the total each time a woman is hired in place of a man. This increase can be considered as a necessary one because of the change in the sex percentages. The actual experience in this plant compares favorably with the experience of the country as a whole. Seven hundred illnesses lasting eight days or more showed that the frequency of illness for men was 96 cases per 1000 employees,

compared with 105.3 cases per 1000 for the whole country, as revealed by figures from the United States Public Health Service.* The frequency of 189 per 1000 for women does not look well when compared with this figure for men. The men in this group of 700 lost an average of 34 days per illness, and the women lost 54 days. Spread over the whole population of the plant, there was a per capita loss of 3.16 days for men and 9.2 days for women. The women lost about 50 per cent more time for each illness than the men. Because of this, and because they had twice as many illnesses as men, their per capita lost time was about three times that of the opposite sex.

Absence from all causes, including sickness, non-industrial accidents, industrial accidents and personal reasons, averaged 17 days for each employee. If the time loss caused by all except personal reasons is deducted, there are still 7 or 8 days chargeable for the most part to unexcusable absence.

When the male employees decreased and the women employees increased, there was also an interesting change in the ages of each group. The men's average age increased $2\frac{1}{2}$ years and the women's age decreased $1\frac{1}{2}$ years, so that the present difference in their ages became 14 years instead of 10. Age as well as sex is probably a factor in the increase.

In fairness to the older women workers, it can be stated that the newly added young women are largely responsible for this bad record. Many of them are at work for the first time, and are not yet accustomed to factory hours and regulations. They do not yet realize that they are no longer in a public school, where they spent 5 hours a day, and had Saturday and Sunday off, and at least a week of vacation every two months. The bad habit of tardiness, also acquired during these school years, still clings to them. Further proof of this is shown in the study of this plant, which reveals that roughly 6 per cent of the women averaging twenty-four years of age accounted for 120,000 hours of the time lost. If each employee of this plant lost time at the same rate, the absenteeism would be double the present rate. There are several reasons why these young people are so frequently absent; these are youth, lack of incentive, lack of responsibility, greater income than needed (they buy spare time with the surplus), and the six-day week, which does not allow them time enough to shop, or to visit the beauty parlor. The typical young woman does not expect to work indefinitely. The factory has no great appeal for

*Galester, W. M. Sickness absenteeism among industrial workers, final quarter of 1942, with a note on the occurrence of Tronchitis and pneumonia, 1931-42. 3 pp. A release from the Division of Industrial Hygiene, National Institute of Health, United States Public Health Service, Bethesda, Maryland.

her and she can see no romance in the job. By her inheritance of sex, she looks forward to a home of her own, and she believes that the day is just around the corner when she will achieve that objective.

An interesting thought in connection with the employment of these younger women, and perhaps some of the older ones, is suggested by the excuse of one of our young married women when brought to task for her frequent absences. Her excuse was in substance, "I have only four or five days a week to give to factory work to help in the war effort, and if that is not enough, so what?" The three or four days lost each month by this woman are charged to absenteeism in the records, and there are probably many more cases just like hers. No doubt this is a large factor in producing the high rates that are now experienced, and the remedy seems to lie in the employment of still larger numbers of women on a schedule of four or five days a week. I do not know that this is a practical thing to do or that it can be done in many plants, but it would undoubtedly be effective in reducing absenteeism.

Dissatisfaction with the work they are doing, lower rates of pay than those that prevail in the factory next door and longer hours than they wish to work probably lead to job shopping on the part of many workers. Part of the time lost in one factory is spent in looking up a job in some other factory. I shall even go farther than that. Part of the time lost in one factory is spent at productive work in another factory by workers who are holding down more than one job at the same time. This, of course, will be remedied by job freezing. It will be interesting to see how many workers are caught between jobs when the new freezing order becomes effective.

All the facts brought forth here put most of the blame on women, and perhaps rightly so, but youth is also a very important factor. The shipyards and plane factories where men predominate also show high rates of absenteeism.

Perhaps it is not fair to measure these women by the standards set by workers during normal times, but I hope that a way may be found to keep them on the job more regularly, at least for the duration of the war.

It has been said that the employment of older people has added to this problem. I do not believe that it has done so to any great extent. The older person is steadier in his attendance than the younger and as a rule does not stay out except for good cause. He cannot develop the speed of younger people and he does not as a rule have so great dexterity in his work, but by his stick-to-itiveness he is contributing to the best of his ability. If the work and the speed of work can be fitted to the older employee, he can become a valuable producer.

* * *

If the reasons given are real factors in producing increased absence from work, time should bring about an improvement. The youngsters who are largely to blame will grow up and finally realize that they are important, and they will eventually do as good a job if not a better one than the older workers are now doing.

Physicians, who are familiar with the weaknesses and emotions of people, should be able to do much to help in correcting these evils. We have more and closer contacts with the worker than any other group or class of people, and we can influence their attitude greatly if we will.

98 Nichols Avenue

THE ROENTGENOLOGIC DIAGNOSIS OF RIGHT-SIDED ENLARGEMENT OF THE HEART

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DURING the last three years we have studied the heart and great vessels by angiocardiography in approximately 270 patients. This involved making serial roentgenograms of the chest following the intravenous injection of 70 per cent Diodrast (Winthrop). The object of the present report is to present a chamber analysis of the cardiac contour in cases with striking right-sided enlargement, and to review critically the criteria for the diagnosis in the light of the intravital visualization of this chamber.

The anatomical basis for the roentgenologic diagnosis of right ventricular enlargement is found in the work of Kirch,¹ who concluded that this chamber acts physiologically as if composed of an inflow tract extending from the tricuspid valve to the apex, and an outflow tract extending from the ventricular apex to the pulmonic valve. He showed experimentally that the earliest response of this chamber to increased pressure was lengthening of the outflow tract. When the strain on the right ventricle was increased and prolonged, dilatation of the inflow tract followed. His post mortem data suggested that this sequence occurred also in man, except that in the presence of a damaged myocardium, enlargement of the inflow tract might precede or accompany lengthening of the outflow tract. To our knowledge, no pathological data confirming the occurrence of this sequence of events have been published. It is a common observation, however, that although marked hypertrophy of the right ventricle without significant dilatation occurs occasionally, ordinarily both are found. In other words, concentric hypertrophy in the right ventricle comparable with that occurring in the left is an unusual finding.

The roentgenological literature has followed the precepts laid down by Kirch. These have been excellently summarized by Schwedel,² the main principles being paraphrased as follows:

The earliest enlargement of the right ventricle occurs in the outflow of this chamber, which bulges anteriorly into the lung-filled triangle of the anterior mediastinum. This is seen earliest in the right anterior oblique position. The first noticeable enlargement in the posterior

position is usually upward and to the left, filling the concavity of the left border between the hub of the aorta and the left ventricle. With additional enlargement the right ventricle extends more and more upward and to the left, occupying more of the middle left cardiac contour, and this segment changes downward.

Inflow tract enlargement follows that of the outflow tract and produces increased depth of the chamber. This is seen best in the left anterior oblique position, where there is an anterior bulge of the lower portion of the anterior contour. The diaphragmatic portion of the heart, chiefly the right ventricle, increases in length. More marked enlargement results in displacement of the interventricular groove posteriorly and then upward on the lower contour. Marked enlargement of the outflow tract may occur without enlargement of the inflow tract. Furthermore marked enlargement of the outflow and inflow portions may occur without enlargement to the right in the posterior view. An attempt to differentiate between enlargement of the inflow and outflow tracts should be made for diagnostic as well as prognostic reasons.

When the cardiac contour is subjected to chamber analysis doubt arises regarding the value of the criteria. This will be illustrated by a consideration of the various conditions in which the right heart is enlarged.

ROENTGENOLOGIC DATA

Emphysema

There is fair agreement in the recent literature that pathologically the right ventricle is usually enlarged in emphysema. In 28 cases of this condition, which we studied also by angiocardiography,³ there was no case in which the heart was more than 10 per cent larger than prediction tables consider normal. Ten cases showed varying degrees of enlargement up to 10 per cent. The remainder were normal or smaller than normal, the smallest being -15 per cent. The middle left cardiac contour was prominent only in some cases, but in many some prominence of the hilar vessels was noted. In the left oblique position, a bulging right anterior curve was the exception. Nevertheless, by angiocardiography, a definite right ventricular dilatation was found in 12 cases. In 12 others, enlargement of the chamber was thought to be present but was not conclusively demonstrated. Several cases that showed the most marked right ventricular dilatation were associated with completely normal cardiac configurations. The reason is suggested by the angiocardiographic

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evidence of right ventricular enlargement, which consists of widening of the right ventricular apex and bulging of the interventricular septum to the left instead of to the right as normally (Fig. 1).

fore could not account for the prominent middle segment. In other words, this criterion may be applied only with the realization that prominence of the pulmonary-artery segment is not necessarily



FIGURE 1. *Emphysema.*

The angiocardio-gram, made in the left anterior oblique position, shows an enlarged right ventricle. The heart is normal in size and shape. The apex is widened and the interventricular septum bulges to the left.

In many cases in which there was no change in the position of the septum, definite left ventricular dilatation was present owing to hypertension or coronary sclerosis, which was most likely a counterbalancing factor. It is quite evident that displacement of the septum due to right ventricular enlargement will not be made out in conventional roentgenography of the heart, and that considerable dilatation can take place without being detectable, although small changes may be demonstrated where serial studies are available. Indeed, right-sided heart failure may appear clinically in emphysema without significant change in the size or shape of the heart, or at most with an increase in the transverse diameter to the left. The position of the interventricular groove described by Nemet⁴ has not been found to correspond accurately to the anatomic groove between the right and left ventricles, and is of limited value in the detection of moderate right-sided enlargement of the heart.

Prominence of the pulmonary-artery segment, which is used by Parkinson⁵ as a criterion of right ventricular enlargement in emphysema, was present in some of our cases, but was shown to be due to actual dilatation of the pulmonary artery in two thirds of them, and to accentuation of the curve resulting from the vertical position of the heart in the remainder. The pulmonic valve was not elevated. Lengthening of the outflow tract there-

due to right ventricular dilatation, even though in emphysema the two findings may occur together.

The greater degrees of enlargement of the right ventricle are better evaluated in connection with cor pulmonale.

Mitral Disease

The statement that a prominent and elongated middle left arc is due to lengthening of the outflow tract of the right ventricle is derived largely from consideration of a mitral configuration. The profound effect of a large left auricle on the entire cardiac contour has apparently not been fully appreciated. It is quite evident from angiocardio-grams made in oblique positions that this chamber enlarges in all dimensions (Fig. 2). As it enlarges anteriorly it presses on the right ventricle and pulmonary artery, so that these structures are stretched and bowed anteriorly. As a result, the pulmonic valve may be elevated in position. The pulmonary artery particularly is elongated and is displaced anteriorly and cephalad, but ordinarily it is not significantly dilated.

In mitral stenosis the middle left segment seen in the posteroanterior view has been shown by angiocardio-gram to consist in most cases of the dilated left auricular appendage or atrium. The left pulmonary artery is seen above the auricle and may constitute a separate arc. The pulmonary artery and conus are demonstrated well within the

cardiac shadow. Evidently, therefore, in the posteroanterior view, prominence of the middle left cardiac segment in mitral disease is not a

ment on the retrosternal space as seen in the lateral view can be explained on the same basis. It is important also to realize that in mitral disease,



FIGURE 2 Mitral Stenosis.

The angiocardigrams in the posteroanterior and left oblique positions show the middle left cardiac contour made up chiefly by the enlarged left auricle (broken outline). The right ventricle and pulmonary artery are stretched and bowed anteriorly.

direct indication of right ventricular enlargement, although hypertrophy and dilatation of this chamber are regularly present when the left auricle is

the widening of the diaphragmatic surface of the heart and the bulging of its right anterior surface can be accounted for in large part by the dilated

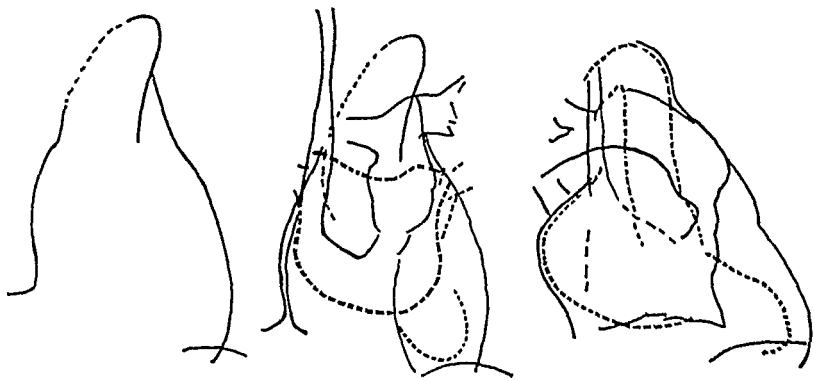


FIGURE 3 Mitral Stenosis and Insufficiency

The angiocardigrams were made in posteroanterior and right oblique positions. The dilated pulmonary artery makes up the middle left cardiac contour only in the right oblique position.

enlarged. On the other hand, in the right oblique position the pulmonary artery is brought into contour because it is bowed anteriorly by the left auricle (Fig. 3). The larger the auricle, the more prominent is the middle left segment. Encroach-

ment on the retrosternal space as seen in the lateral view can be explained on the same basis. It is important also to realize that in mitral disease,

(Fig. 4). Hence in mitral stenosis the findings observed in the left anterior oblique position are not necessarily an indication of the degree of right-

Cor Pulmonale

The conclusion that a bulging pulmonic segment is primarily due to dilatation of the pulmo-

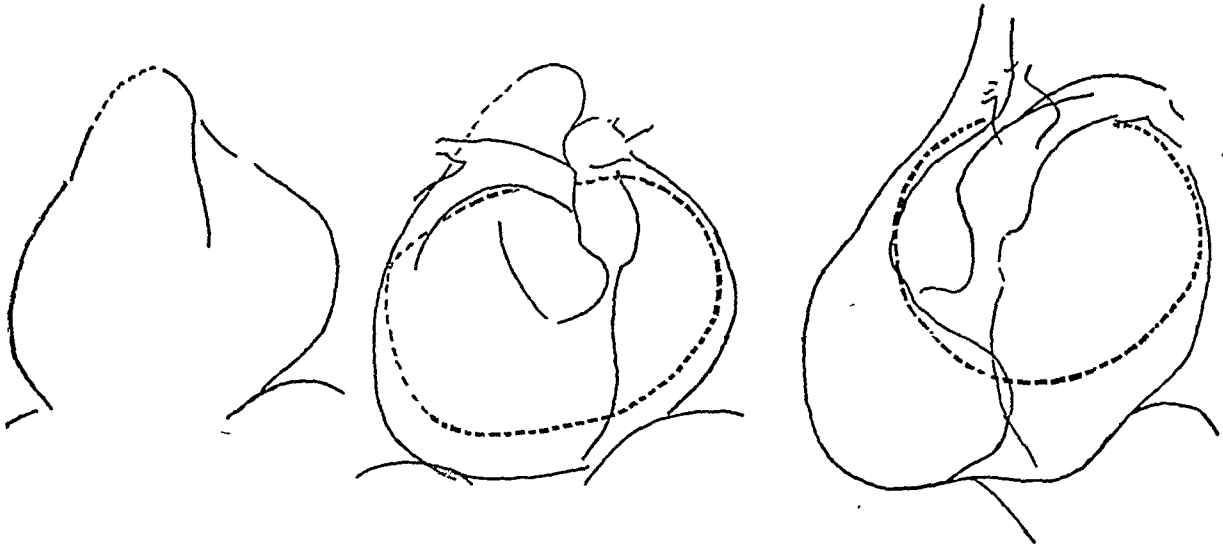


FIGURE 4. *Mitral Stenosis with Giant Left Auricle.*

Angiocardiograms, made in posteroanterior and left oblique positions, illustrate the extent to which the heart is distorted and enlarged by the huge left auricle.

sided enlargement of the heart. The displacement effect also explains enlargement to the left, in spite of the fact that a small atrophic left ventricle

nary artery is tested more conclusively in the cases of cor pulmonale with unquestioned and striking right ventricular enlargement. Two cases were

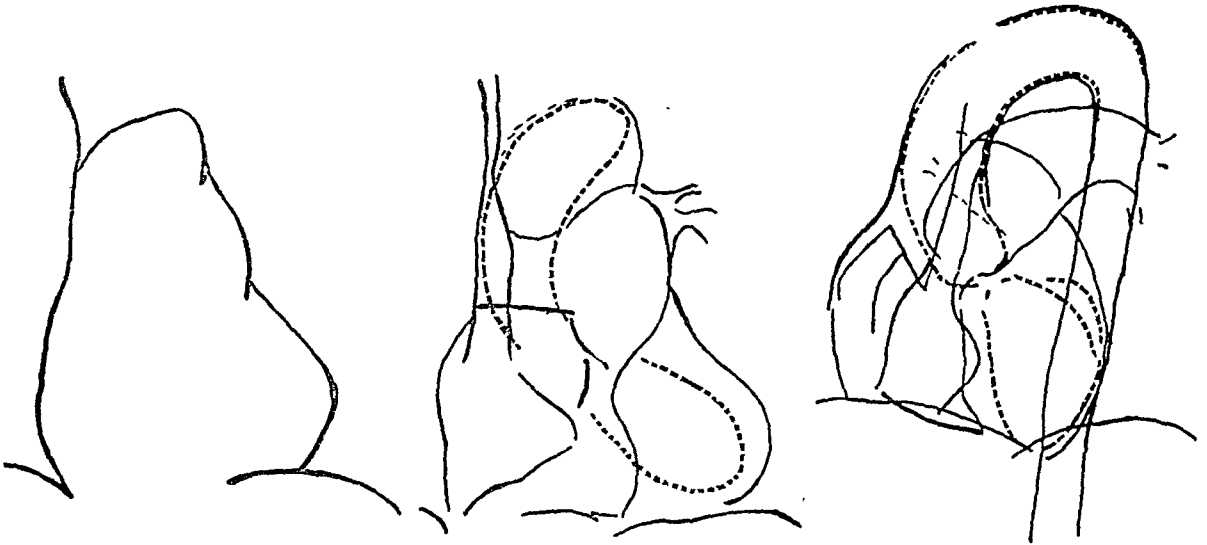


FIGURE 5. *Cor Pulmonale.*

The angiocardiograms were made in posteroanterior and left oblique positions. The bulging middle left segment is made up by a dilated pulmonary artery. The pulmonary valve is not elevated significantly.

may be present. Ordinarily, however, this can be evaluated by the shape of the lower left contour and the position of the junction of middle and lower left arcs.

subjected to angiocardiography, one of which was subsequently examined post mortem. In these cases the heart was enlarged in its transverse diameter, the enlargement being mainly to the left

in the posteroanterior view. There was a marked bulge in the middle left cardiac segment. In the left-anterior-oblique position the diaphragmatic surface of the heart appeared increased in size and the right contour bulged anteriorly. However, angiocardiograms (Fig. 5) show clearly that the major reason for the prominent pulmonic seg-

mainly to the left, and the base of the heart below the pulmonary segment may be widened. When, as occasionally happens, pulmonic stenosis occurs with dilatation of the pulmonary artery, a bulging middle left cardiac segment appears (Fig. 6). These same conclusions are reached in comparing the configurations in tetralogy of Fallot (Fig. 7)



FIGURE 6. Pulmonic Stenosis, with Dilatation of the Pulmonary Artery.

The angiocardiograms were made in the posteroanterior and left oblique positions. The middle left arc is made up by the dilated pulmonary artery, and also by the adjacent descending branch of the left pulmonary artery. The large right ventricle contributes to the widened base.

ment was marked dilatation with tortuosity of the pulmonary artery. The pulmonic valve is seen deep in the shadow of the heart and is moderately elevated. The pulmonic conus, which we define as the infravalvular portion of the right ventricle, does not approach the left cardiac contour. Hence, although the outflow tract of the right ventricle is lengthened, the increase is in proportion to the general increase in the size of the cardiac chamber. The chamber dilatation results in some pulmonary-artery elevation and contributes to its tortuosity, but it is not a primary factor in the production of the prominent middle left cardiac contour. However, it may contribute indirectly to the widening of the base of the heart below the pulmonary-artery segment, and thus to a straightening of the left middle segment.

Pulmonic Stenosis

Another excellent example is afforded by cases of pulmonic stenosis in which the right ventricle is enlarged but the pulmonary artery is not dilated. In these, the middle arc of the left contour is neither exaggerated nor lengthened. Right ventricular enlargement in these cases produces an increase in the transverse diameter of the heart

and the Eisenmenger complex. When the right side of the heart is huge, however, the cephalad enlargement, which occurs in proportion to the dilatation in other directions, displaces the pulmonary artery cephalad and produces a prominent pulmonic segment without striking dilatation of the pulmonary artery.

Inflow-Tract Enlargement

Enlargement of the heart to the right in the posteroanterior position, as well as the bulging right anterior contour seen in the left oblique position, is usually due to the presence of a large right auricle. The right ventricle rarely approaches the contour. However, enlargement of the right ventricle may be assumed to be present when a large right auricle is found, except in rare cases of isolated tricuspid stenosis. It follows, therefore, that enlargement to the right usually occurs when heart failure is present. Isolated right-sided heart failure is rare clinically. In the usual case, therefore, enlargement of all chambers may be expected and is ordinarily found, being manifested as enlargement of the heart to the right and left with widening at the base. An antecedent or predominant right-sided enlargement is apt to be associated

with dilatation of the pulmonic artery, which, combined with enlargement of the right ventricle in all diameters, is associated with a prominent middle left segment. In occasional cases, a huge left ventricle may confuse the analysis by displacing the entire heart to the right.

DISCUSSION

Moderate right ventricular enlargement is not associated with a prominent middle left cardiac

enlargement of the heart to the right is usually of grave prognostic significance and occurs ordinarily in the presence of heart failure. On rare occasions a huge left ventricle may confuse the picture by displacing the entire heart to the right.

When the prominence that occurs simply as the result of a vertically placed heart is excluded, a bulging middle left cardiac segment has been found to be due to dilatation of the pulmonary artery or to an enlarged left auricle that dis-

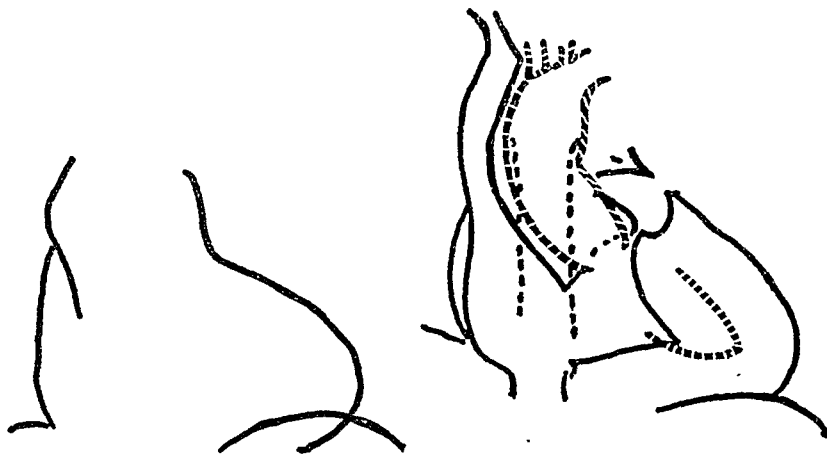


FIGURE 7. Tetralogy of Fallot.

The angiocardioqram, made in the posteroanterior position, shows the combination of a large right ventricle and small pulmonic artery. The middle left arc is not bulging, but the base of the heart is widened.

arc or with a bulging of the right anterior curve in the left oblique position unless additional chambers or vessels are enlarged. When right ventricular enlargement alone is present, the significant finding is an increase in the transverse diameter of the heart, mainly to the left. However, when in addition to the cause of right-sided enlargement, hypertension or coronary sclerosis is present, resulting in left ventricular hypertrophy and dilatation, the two ventricles cannot be differentiated easily from the roentgenologic examination, and indeed usually both are enlarged. When increasing left ventricular dilatation can be excluded or minimized on clinical grounds, a progressive enlargement of the heart to the left as shown on serial roentgenograms is indicative of right ventricular dilatation. Dilatation of the pulmonary artery may be taken under these conditions as additional evidence that the right ventricle is enlarged.

In the absence of left auricular enlargement, when the heart enlarges to the right and the right anterior contour bulges, dilatation of the right auricle in addition to that of the right ventricle may be assumed. Hence, under these conditions,

place the pulmonary artery. The outflow tract of the right ventricle does not necessarily contribute to the prominence of this segment. However, since it is lengthened in proportion to the general dilatation of the chamber, it may act indirectly by displacing the pulmonary artery cephalad and to the left. In this way, the base of the heart below what is conventionally called the pulmonary-artery segment may be widened, and the entire middle left arc may be lengthened. Most conditions in which actual dilatation of the pulmonary artery is present are associated with right ventricular enlargement. Hence the demonstration roentgenologically of dilatation of the pulmonary artery may ordinarily be assumed to indicate dilatation and hypertrophy of the right ventricle, but the two are not necessarily proportional.

In mitral disease, the large left auricle displaces the right ventricle anteriorly and to the right. The pulmonary artery is elongated and elevated anteriorly and cephalad. Hence enlargement to the right, widening of the diaphragmatic portion of the heart, bulging of the right anterior contour as seen in the left oblique position and a prominent elongated middle left contour are not indications

in mitral disease of the degree of right-sided enlargement, even though varying degrees of enlargement are regularly present. The major portion of the middle left cardiac contour in the postero-anterior position is due to the large left auricle. In the same way, widening of the heart to the left does not necessarily indicate left ventricular enlargement.

The present study has not resulted in a simple method for the demonstration of right ventricular enlargement. However, it is hoped that a more rational and accurate interpretation of the roentgenologic findings in right heart enlargement is now available. The results are based largely on the angiocardigraphic investigation of 270 cases. In general, the results coincide with the analyses obtained by Laubry, Cottenot, Routier and Heim de Balsac⁶ following post-mortem injection of the heart in cadavers.

SUMMARY

The roentgenologic configuration of the heart in various diseases associated with right-sided enlargement has been analyzed with the aid of angiocardigraphy. It was found that considerable enlargement of the right ventricle can occur without any demonstrable change in the size or shape of the heart unless serial roentgenograms are available. Widening at the apex with convexity of the interventricular septum to the left instead of to the right found by angiocardigraphy

cannot be seen in the conventional roentgenologic examination. With increasing dilatation of the right ventricle the transverse diameter increases to the left. Finally, especially when right auricular dilatation takes place, there is cardiac enlargement to the right and anteriorly as well as elevation of the right cardiac-supracardiac junction.

Right-sided enlargement of the heart is often associated with dilatation of the pulmonary artery. Hence, in certain diseases, prominence of the middle left cardiac segment is an indirect indication of right ventricular dilatation.

In mitral disease the large left auricle displaces the right ventricle anteriorly and to the right. The pulmonary artery is elongated and elevated anteriorly and cephalad. The convex or straightened middle left segment of the cardiac contour is due primarily to the large left auricle. The degree of right sided enlargement in this condition may be difficult to evaluate.

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PROGNOSIS IN CASES OF SEROFIBRINOUS PLEURISY*

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IT IS generally accepted that the majority of cases of so-called "idiopathic serofibrinous pleurisy" are tuberculous in origin.¹⁻⁴ Follow-up studies on series of such cases have been reported. Hamman⁵ collected 562 cases, in 30 per cent of which the patients later developed tuberculosis. Kallner⁶ found that in a period of twenty years after pleurisy, 39 per cent of 690 patients developed tuberculosis and at least 22 per cent died. Korn⁷ reported that 48 per cent of 514 patients were later found to have pulmonary tuberculosis. Miller and Wallgren⁴ state that between one third and one half of all adults with pleural effusion go on to pulmonary tuberculosis within the next few years. Thus, it is recognized that simple pleurisy with effusion is a disease with a serious prognosis.

The present study is concerned with the prognosis in a series of 137 patients with this condition admitted to the Edward J. Meyer Memorial Hospital between 1929 and 1939. A reliable follow-up for three to thirteen years was obtained on 111 patients. The data on the latter group are analyzed as to the clinical, laboratory and roentgenological findings and the subsequent occurrence of tuberculosis.

DATA

Age, sex and color. There were 77 white patients—49 males and 28 females—and 30 Negroes—20 males and 10 females. Four patients were male American Indians.

Tables 1 and 2 show all cases arranged in age groups. The median age of the white males was

TABLE 1. Age and Prognosis of White Patients.

AGE yr.	TOTAL NO. OF CASES	CASES OF TUBERCULOSIS	
		NO.	PER CENT
Under 10	4	0	0
10-19	13	3	23
20-29	22	7	32
30-39	12	3	25
40-49	16	6	38
50 and over	10	0	0
Totals	77	19	25

thirty-seven years and of the white females twenty. The median age of the male Negroes and Indians‡ was thirty-one, and that of the women was twenty-

nine. For the combined group of males in the series the median age was thirty-three, and that of the females twenty-one.

Occupation and socioeconomic status. The economic status of the majority of adult patients placed them in the low-income group.§ Most of

TABLE 2. Age and Prognosis of Negro and Indian Patients.

AGE yr.	TOTAL NO. OF CASES	CASES OF TUBERCULOSIS	
		NO.	PER CENT
Under 6	1	0	0
10-19	5	4	80
20-29	10	6	60
30-39	12	6	50
40-49	4	1	25
50 and over	2	2	100
Totals	34	19	56

the men were unskilled workers from the heavy industries in and about Buffalo. Seven of the women were student nurses; most of the women were housewives.

Tuberculin sensitivity and sputum examination. Data on tuberculin (Mantoux) tests were available in only 30 patients. Of these, 28 gave positive and 2 gave negative reactions. All patients had multiple sputum examinations, and none were positive.

Onset, fever and clinical course. Of the 111 patients with adequate follow-up, 55 stated that the onset of their illness was somewhat insidious and 56 that it was sudden and explosive. The clinical picture was typical of serofibrinous pleurisy, with pain in the chest, fever, malaise, dyspnea, anorexia and loss of weight. The blood pressures were within normal limits. Almost all patients had an elevation of body temperature of 1 to 3°F., which lasted for approximately four weeks. Some of the young Negro patients ran a fever of 4 to 5°F. for many weeks. Eleven white and 2 Negro and Indian patients, however, exhibited very little fever. Although they undoubtedly had a fever prior to admission, it was not a chief complaint. Clinically, the latter group were not very ill, although two of them later developed tuberculosis. These cases seem to correspond to the ambulant pleurisies of Miller and Wallgren.⁴ Fifty-three of the patients had a right-sided and 58 a left-sided effusion. The average period of hospitalization was seventy-five days.

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‡The four Indians are included in one group because of their similar biologic reaction to tuberculosis and for statistical convenience.

§The Edward J. Meyer Memorial Hospital is a municipal charity institution.

Blood-cell counts. The average white-cell count was 9870 (range 5000 to 23,000). The average differential blood count was as follows: neutrophils, 72 per cent (range 54 to 87 per cent); lymphocytes 24 per cent (range 11 to 40 per cent); monocytes 4 per cent (range 1 to 10 per cent). Twenty patients showed from 1 to 4 per cent eosinophils.

Röntgenology. Each patient had at least one roentgenogram of the chest while in the hospital. In each case there was a density characteristic of fluid, varying from one third to almost the entire hemithorax. Serial roentgenograms showed a gradual disappearance of the fluid. In the follow-up period, x-ray films of the chest were taken at varying intervals over a number of years. Patients with both pleurisy and roentgenologically demonstrable parenchymal tuberculosis were not used in this study.

Character of effusion. A diagnostic thoracentesis was performed in almost every case. Data on the physical, cytological and bacteriological character of the fluid were available in 86 cases. The fluids were usually clear and amber or straw-colored. The specific gravity ranged between 1.017 and 1.031. In only 1 case was the specific gravity below 1.018. Differential cell counts showed a predominance of lymphocytic cells. A Rivalta test was positive in all cases. All the fluids were cultured for secondary organisms, and none were positive. Unfortunately, cultural methods for tubercle bacilli were not being used at the hospital at the time. It was possible to locate results of injection of the fluid in guinea pigs in only 66 cases. Nineteen of these were positive and 47 were negative.

Treatment. The patients were hospitalized on several medical wards and therapeutic management was conducted by a number of physicians. In spite of this, a fairly uniform method of treatment was followed. The patients were maintained on strict bed rest during the febrile period of approximately four weeks. During this time symptomatic and palliative measures were used. Thoracentesis was performed for diagnosis and when marked cardio-respiratory embarrassment was manifested. After subsidence of the acute phase the patient was kept on a modified bed-rest program and was usually given a series of Alpine-lamp (ultraviolet-ray) treatments to the entire body. The patients were then discharged to their homes to continue the modified bed-rest program and to visit the outpatient chest clinic for a follow-up. Many of the patients, however, did not pursue a rest program and returned to their former occupations.

Subsequent occurrence of tuberculosis. Of 111 patients followed for three years or longer, 38 (34

per cent) developed tuberculosis—in most cases pulmonary tuberculosis. Three patients had tuberculous meningitis, and 3, acute miliary tuberculosis; there were 1 case each of tuberculosis of the hip and of the knee and 2 cases of Pott's disease.

TABLE 3. Onset of Tuberculosis.

PERIOD AFTER PLEURISY	WHITE PATIENTS	NEGRO AND INDIAN PATIENTS	TOTAL CASES NO	PER CENT
1 yr				
1	3	5	8	21
2	6	7	13	34
3	3	2	5	13
4	1	1	2	5
5	2	3	5	13
6	0	0	0	0
7	2	1	3	8
8	2	0	2	5
Totals	19	19	38	

Twenty-five per cent of the white patients and 54 per cent of the Negro and Indian patients eventually developed tuberculosis. Thirty-three of the entire series developed tuberculosis within five years of the pleurisy (Table 3).

Deaths. Twenty-seven (71 per cent) of the 38 patients who developed tuberculosis died. Autopsies were made in 10 cases. The majority of patients died from tuberculosis of the lungs, although involvement of other organs was not uncommon. In addition to those patients who died from tuberculosis, there were 2 who died suddenly during the acute phase of the pleurisy. In both cases the clinical picture seemed to be that of acute cardiac failure, but proof is absent, since permissions for autopsy were not obtained.

DISCUSSION

The study of a group of cases of serofibrinous pleurisy over a period of years cannot but thoroughly convince one that many, if not all, cases are of tuberculous origin. Autopsy studies on patients who have died during the course of idiopathic serofibrinous pleurisy have shown that the pleura is inflamed and edematous, weeping a watery, amber-colored fibrinous exudate and often studded with tiny grayish tubercles.^{3, 8, 9} Attention is thus directed to the underlying disease process of the pleura and lung as well, rather than to the fluid, which "is essentially an incident in the wider disease—it is the disease behind the fluid which is of primary significance."⁴ The therapeutic implications of this are quite obvious, for the mere disappearance of the exudate does not signify a healed underlying lesion. One can speculate concerning the sources of the bacilli on the pleura.³

Did they come from a subpleural caseous focus, or are they bacilli originating from a caseous lymphadenitis in the mediastinum or elsewhere? Regardless of the exact location of the source of the bacilli, the practical consideration seems to be that there is a focus of active tuberculosis somewhere in the body and itself in need of treatment. Hence, treatment must be directed not only to the pleurisy itself but to the original active focus of tuberculosis. That this conception of the basis of treatment has not always been shared is attested by the various methods of treatment that have emanated largely from European clinics. The use of calcium chloride to reduce fever and to produce diuresis, thus causing absorption of the fluid, has been frequently advocated.¹⁰⁻¹³ Others recommend vaccines,¹⁴ radium,¹⁵ blood,¹⁶ iodine,¹⁷ milk¹⁸ and various drugs,¹⁹ to be given parenterally. Lassen²⁰ uses ultraviolet rays and Caracciolo²¹ injects adrenalin into the effusion. In all cases, treatment is directed chiefly to the fluid rather than to the underlying pathologic process.

A prominent feature of the present series is that most of the patients belonged to the lower socioeconomic stratum, in which tuberculosis is known to be most prevalent. They not only came from an environment favorable for the development of tuberculosis, but returned to the same surroundings after their acute pleurisy had subsided. Furthermore, the group as a whole did not receive the benefit of adequate bed rest or sanatorium care following the acute phase of the illness. After roughly ten weeks of hospitalization the patients returned home to "normal" activities, even though they were advised to rest and "take a cure." The importance of this is seen at once by examining the reports of Trudeau²² or of Jacquelin and Mallet.²³ Their patients not only came from the upper economic stratum but after subsidence of the fever were given an adequate program of sanatorium care. Hence, the low incidence of tuberculosis in subsequent years in their series is explainable. In Trudeau's series of 83 patients with pleurisy, including 29 that also had slight apical parenchymal involvement, only 12 developed tuberculosis. Trudeau concludes from this that "the prognosis of pleurisy with effusion . . . is excellent in patients receiving at least four months of sanatorium care." Anderson²⁴ similarly believes that pleurisy is a relatively light and curable phase of tuberculosis.

In the reported series, the median age of the male patients was twelve years higher than that of the females. This tends to conform to the age disparity between males and females noted in large series of tuberculous patients.²⁵

The racial factor seems to be of distinct significance in the prognosis of such patients. In the present series more than twice as many Negro and Indian as white patients subsequently developed tuberculosis. In this connection Pinner²⁶ has demonstrated the greater frequency of hematogenous, lymphatic and exudative tuberculosis in the Negro than in the white man.

The clinical picture in this series corresponded to textbook descriptions of the disease.^{27, 28} The duration of fever agreed with Amberson's²⁸ observations (four weeks). Especially in the group of Negro patients the onset was often so explosive that a preadmission diagnosis of pneumonia was frequently made. Exceedingly rapid accumulation of fluid was often seen, and as previously noted, 2 patients died during the acute phase of the illness. In the cases in which the onset was insidious, premonitory symptoms, especially pain in the chest, were often noted.²⁹ Blood-pressure determinations and blood counts were found to be of little prognostic value. Sartorari,³⁰ however, finds eosinophilia a favorable prognostic sign in pleurisy.

Probably the most complete study of the fluid in pleurisy is that of Pinner,³¹ who found that neither chemical nor cytological nor serologic data *per se* afford dependable diagnostic or prognostic criteria. The data from our fluid examinations tend to bear out these observations. All fluids were found to be negative on culture for secondary organisms. Only about one third of the guinea-pig tests were positive. There are undoubtedly several reasons for this. Pinner,³¹ in commenting on this involved question, cited the numerous reports on atypical and filterable forms of tubercle bacilli. European students^{3, 6, 8, 32} of the subject believe that many of these pleurisy, on the basis of an antigen-antibody reaction, are allergic (tuberculous) in nature, so that tubercle bacilli cannot be recovered from the fluid. Also, the volume of fluid used for the guinea-pig test may play an important part in the result³³; that is, the larger the amount used, the greater the chance of obtaining a positive result. In the present series a small amount of fluid was generally used for inoculation. Evidently there was no positive correlation between the guinea-pig test and the subsequent occurrence of tuberculosis.

The question arises whether, in the final analysis, treatment or management of the afflicted patient is not of paramount importance and a major factor in his ultimate fate. The excellent results obtained by Trudeau²² and others²³ support this thesis. Pinner³⁴ writes that there is excellent evidence that pleurisy when properly treated has a relatively good prognosis. As clearly stated by Amberson,²⁸ a patient with serofibrinous pleurisy

should be regarded as having *active tuberculosis*. The patient is certainly not cured when the fluid has been absorbed or removed and when the temperature has become normal. After the acute phase of the illness a sanatorium type of program should be followed for at least six months. The patient should then remain under careful medical supervision for at least five years.²⁵ In this way the underlying tuberculous focus in the body will have an opportunity to become thoroughly arrested, and the patient can have added protection from eventual pulmonary or other forms of tuberculosis. As Jacqueroed³⁰ aptly states, serous pleurisy, like an initial hemoptysis, may be regarded as a "happy accident" calling attention to the need for treatment while the prognosis is yet good.

SUMMARY AND CONCLUSIONS

One hundred and thirty-seven patients with so-called "idiopathic serofibrinous pleurisy" have been studied, chiefly in regard to the subsequent occurrence of tuberculosis. It was possible to obtain a reasonably adequate follow-up on 111 patients. None of these had sanatorium care after the acute phase of the pleurisy. Twenty-five per cent of the white and 56 per cent of the Negro and Indian patients later developed tuberculosis. Of the combined group of patients, 38 (34 per cent) developed tuberculosis. Twenty-seven of these died from the disease. Idiopathic serofibrinous pleurisy when not adequately treated is evidently a disease with a serious prognosis.

Apart from the racial factor, the prognosis seems to be influenced chiefly by the management of the patient. This is borne out by reports in the literature showing that, when properly treated, pleurisy has a relatively good prognosis. Treatment should be based on a knowledge of the cause, pathogenesis and pathology of the disease. Hence, the case should be treated as one of active tuberculosis. A sanatorium type of program should be followed for six months to a year after the acute phase of the illness, and the patient should then be kept under clinical and roentgenographic observation for at least five more years.

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MEDICAL PROGRESS

EPIDEMIOLOGIC ASPECTS OF FOOD-BORNE DISEASE (Continued)

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Paratyphoid Fever

THE *Salmonella* group of bacteria, formerly called the paratyphoid bacilli, is composed of many species, and new ones are still being isolated. Some species, according to Dack,² produce disease only in man, whereas others produce disease in animals and the infection may be transferred to man, either directly by food of animal origin or through food contaminated by the excreta of rats or mice.

Edwards and Bruner,⁶⁷ at the Kentucky Agricultural Experiment Station in Lexington, Kentucky, typed 3090 cultures of *Salmonella* from 2285 outbreaks in man and animals from thirty-six states. Fifty-nine types were encountered; of the cultures isolated from man, 99 per cent were members of Groups A, B, C, D and E of the Kauffmann-White schema. The frequency of the occurrence of the various types in man and animals is strikingly similar. Some of the species are confined largely to man and others largely to animals, but the great majority are found in a number of animal species and in man, a fact that emphasizes the lack of host specificity of most *Salmonella* types. The possibility of direct transference of *Salmonella* infection from animal to man is obvious. On the other hand, the isolation of bacilli of this type from such a large number of normal human carriers indicates how often outbreaks of *Salmonella* organisms may originate from food handlers who are carriers of bacilli.

Welch et al.⁶⁸ conducted laboratory experiments on the role of rats in the spread of *Salmonella* infections. The excreta of rats that were naturally infected with *S. enteritidis* when held at room temperature contained living organisms for at least one hundred and forty-eight days. Cross-infection between mice and rats took place in cages. These authors examined 420 specimens of murine excreta, 80 mouse and 340 rat, collected from all parts of the country and found only 1.2 per cent positive for *Salmonella*. Certain rat exterminators, known as "rat virus," contain *Salmonella* organisms. This is a dangerous procedure, since the *Salmonella* is

pathogenic for man. Spray⁶⁹ reported an outbreak in 1926 involving 135 cases traced to milk presumably contaminated with "rat virus."

Ostrolenk and Welch⁷⁰ experimented with the house fly (*Musca domestica*) as a vector of *S. enteritidis*. Flies fed on food infected with this organism are capable of infecting other flies, as well as food, water and miscellaneous surfaces with which they come in contact. The organism apparently survives in the fly for the duration of its life—about four weeks. These authors observed the transfer of *S. enteritidis* from flies to mice and their retransfer from mice to flies. Moreover, fly eggs planted in mash and infected with *S. enteritidis* resulted in infected maggots, pupas and adults. In view of all these experiments, foods should be protected from both rats and flies, since these may act as vectors of *Salmonella*.

Rubin et al.⁷¹ reported the finding of thirteen types of *Salmonella* in the mesenteric lymph glands of apparently normal hogs in Lexington, Kentucky. Of forty lots containing 25 animals each, nineteen (47 per cent) gave positive cultures. Fifty hogs were examined individually; 5 (10 per cent) yielded *Salmonella*. Cherry et al.⁷² cultured 250 samples of meat from fifty-eight retail markets in Lexington. Of 170 samples of pork and 2 mixtures of beef and pork, 6.2 per cent yielded *Salmonella*; 2.5 per cent of 64 samples of beef yielded *Salmonella* whereas 11 samples of lamb gave negative results. Eight types of *Salmonella* were isolated. These authors were convinced that the animals themselves were the source of the *Salmonella*, since there was no correlation between the sanitation of the retail markets and freedom from organisms.

The classification of the *Salmonella* (paratyphoid) group was initiated by White and was further extended by Kauffmann.⁷⁴ In 1934, a subcommittee of the International Society for Microbiology⁷⁵ standardized the terminology. Before the outbreak of the present war, an international *Salmonella* center was established under the auspices of the Commonwealth Fund at Copenhagen by Dr. Thorvald Madsen. A detailed description of *Salmonella* typing can be found in the second edition of *Bacteriology and Immunity* by Topley and Wilson.⁷⁵ Edwards and Bruner⁷⁶ studied the biochemical and serologic varieties of *S. typhi*

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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murium, and the beta phases of the genus *Salmonella*, thereby obtaining two new types,⁷⁷ *S. hartford* and *S. urbana*. The value of *Salmonella* typing in the Connecticut State Department of Health Laboratory is described by Boran et al.⁷⁸ During forty-five months, a total of 358 cultures were typed; 43 per cent of all new isolations were strains of animal origin, representing two types, *S. typhi murium* and *S. schottmuelleri*. The carrier state in man was rarely prolonged either in convalescents or in healthy persons, and the chronic carrier state was by no means so frequently found with animal strains as with strains of human origin. These authors conclude that *Salmonella* typings can save time and effort in the ensuing epidemiologic investigation by demonstrating the relative importance of looking for the human carrier and establishing a chain of events leading from the infected or carrier animal to man.

Savage,⁷⁹ in a study of *Salmonella* infections, concluded that the presence of the organisms in a stool of a patient means an active infection or the carrier state. The different types of *Salmonella*, he states, are serologically distinct, produce no considerable amount of cross-immunity, and cause characteristic pathologic manifestations. Three types of clinical pictures predominate: continued fever (enteric), acute gastroenteritis (food poisoning) and general infection (septicemic). *Salmonella* bacilli cause disease in man, animals and birds; one must therefore look to *Salmonella* animal diseases for sources of food poisoning. *S. paratyphi A*, *S. paratyphi B* and *S. schottmuelleri* produce an enteric type of disease; *S. aertrycke* and *S. enteritidis* cause gastroenteritis, the latter occasionally producing a septicemia; *S. enteritidis* may produce any of the three types; *S. suipestifer* causes gastroenteritis or septicemia.

Hinden⁸⁰ describes an outbreak due to *S. aertrycke* among children of an English hospital ward. Of 14 in the ward, only 3 bottle-fed babies escaped; 11 children, 2 attending physicians and 11 nurses were ill with diarrhea. The author states that there were 299 outbreaks of *Salmonella* food poisoning affecting 4418 persons, with 102 deaths, between 1923 and 1937 in England, an annual average of 20 outbreaks. *S. aertrycke* was responsible for 169 of these.

Savage⁸¹ made an epidemiologic study of paratyphoid fever in Great Britain. There were 40 outbreaks from 1923 to 1941, inclusive, with a mortality of 1.76 per cent. The incubation period averaged seven to twenty-four days. Ice cream was the vehicle responsible for most cases among children. Sixty per cent of the outbreaks started in May, June or July. Cream was the vehicle in 40 per cent and food was responsible for 80 per

cent. Water-borne paratyphoid fever was comparatively rare. Savage brings out two most important epidemiologic factors: if the vehicle containing the bacteria was kept for long periods in warm weather, the attack rate was high; and the source of most of the outbreaks was an ambulant unrecognized or subclinical case.

An outbreak due to *S. aertrycke* from duck eggs that involved 55 boys and 16 adults in an orphanage in this country is described by Brown and his associates.⁸² The eggs were used in the preparation of rice pudding. The same organism was isolated from the feces of nine ducks and from the oviducts of two; the blood of three ducks gave positive agglutination tests. Scott⁸³ describes 7 British outbreaks in which duck eggs were the vehicle of infection. The largest outbreak in this series involved more than 300 persons, with 1 death, the food being ice cream made with duck eggs. *S. aertrycke* was responsible for these outbreaks; this organism can penetrate the shells of duck and hen eggs when applied and kept moist.

S. typhi murium was isolated by Mosher⁸⁴ from a turkey and turkey dressing served in a mental institution; there were 238 cases and 1 death. The manner of infection of the turkey was not ascertained. One patient continued to carry the organism for eighteen weeks.

An account of recent outbreaks of *Salmonella* infections in South Africa is given by Gear et al.⁸⁵ Four cases due to *S. bacilly* are described by Wyllie,⁸⁶ who also reviews the literature on this strain.

Smoked whitefish was responsible for an outbreak of 34 cases and 1 death in New York City in 1934. Kleeman et al.⁸⁷ reported a second outbreak in July, 1940, resulting in 47 cases and 2 deaths in New York City and 17 cases in upstate New York. Smoked fish—carp, whitefish and butterfish—was purchased from twelve different Brooklyn neighborhood delicatessens and was traced through a wholesaler to a smokehouse in upstate New York. Samples of ditch water, the drainage from the washing, soaking and salting vats, contained *S. typhi murium*. The same organism was isolated from 14 customers—(patients), 3 food handlers (patients), 1 wholesaler (a patient), 1 of the processors, who was not ill, and 5 samples of the smoked fish.

In discussing the treatment of clinical dysentery with sulfathiazole in children, Rubens, Kaplan, Borovsky and Blatt⁸⁸ bring out three interesting facts. Their series of cases at the Cook County Hospital, Chicago, consisted of 9 children with negative and 8 children with positive stool cultures of *Shigella* and *Salmonella* who were treated with sulfathiazole. A control series of 16 children

with negative and 13 with positive stools were not given the drug. Patients with clinical dysentery and with positive stool cultures responded to sulfathiazole better than did the group with negative stool cultures. The duration of disease after sulfathiazole treatment was 2.9 days in the treated patients and 4.7 in the untreated patients. Patients with clinical dysentery and positive stool cultures who were treated with sulfathiazole had diarrhea of shorter duration than did those not treated, the durations in the treated and untreated cases being 2.9 and 8.8 days, respectively. These authors administered 1.5 gr. of sulfathiazole per pound of body weight per day, in six equal doses every four hours.

Bacillary Dysentery

Stebbins,⁸⁰ of New York, considers bacillary dysentery a serious problem, especially in small villages and rural areas, where it is more prevalent than it is in urban areas. The ordinary sanitation methods that resulted in the lowering of typhoid-fever rates have not been effective in lowering the incidence of bacillary dysentery. Annually many localized epidemics occur, especially in summer resorts and institutions. In New York, two types, Flexner and Sonne bacilli, are of about equal importance. Proper sanitation of milk, water and food supplies must be instituted to control this disease. Block, Tarnowski and Greene,⁹⁰ of Illinois, declare bacillary dysentery to be even more serious than is typhoid fever, since it is more prevalent and disabling and has a higher mortality. These authors discuss the methods of dissemination by unrecognized cases, by mild or severe clinical cases and by temporary or chronic carriers. According to Ouyang,⁹¹ the disease is extremely prevalent in China. He studied 315 cases in Chinese children from birth to eleven years of age, obtaining the causative organism in 67 per cent of the cases. This high prevalence of bacillary dysentery in countries with primitive sanitation is to be expected. Guidote,⁹² of Manila, cites the reported incidence for 1938 in the Philippines: 40,503 cases and 16,034 deaths from typhoid fever, dysentery and diarrhea or enteritis. Of these deaths 12,158 (76 per cent) were caused by diarrhea or enteritis alone. The peak of morbidity and mortality was in June, July and August. The incidence and mortality were highest in the age group from birth to four years. Guidote believes that primitive sanitation, especially open latrines, are responsible for this high incidence. In Manila, food is the main vehicle for the spread of these diseases.

Watt, Hardy and DeCapito⁹³ state that convalescent and passive carriers of dysentery bacilli oc-

cur commonly. In 103 positive cases, 82 patients (80 per cent) were convalescent carriers described as harboring the organisms after clinical recovery. The average duration of illness was eleven days. The average minimum duration of infection was twenty-seven days, and known convalescent carriers continued positive for an average of thirty-four days. These authors found that the average illness due to Flexner infection was more prolonged than that due to Sonne or Newcastle. They conducted 6324 survey stool examinations in New Mexico, Georgia and Puerto Rico; 239 patients (3.8 per cent) were carriers of dysentery bacilli. This high incidence is in contrast to New York City, where, of 1659 stools examined, only 2 (0.1 per cent) were positive. This difference in carrier rates is in direct proportion to the incidence of the disease in these areas and to the advancement of environmental sanitation.

Kazarnovskaya and Soloveva⁹⁴ state that in hemorrhagic colitis of children, cultures of the stool, if taken often enough, will demonstrate the presence of dysentery bacilli. These authors emphasize the necessity of comparing the results of bacteriologic and coprologic examinations before deciding that a child has ceased to be a carrier. About 65 per cent of the patients are free of dysentery bacilli after three weeks.

Felsen⁹⁵ illustrates the importance of *Shigella* organisms as the cause of diarrhea by citing the data for New York. In 1933, there were 625 reported cases of bacillary dysentery and 17,042 cases of unclassified diarrhea. In 1940, there were 19,152 cases of bacillary dysentery and only 1484 of unclassified diarrhea. New types or strains of dysentery bacilli are being recognized; seven were discovered between 1933 and 1940. For example, Hardy et al.,⁹⁶ in 1940, reported the isolation of the Newcastle bacillus, which had formerly been found only in Africa, England, India and South America, from three different areas in the United States—New Mexico, Georgia and New York City.

Macumber⁹⁷ studied 263 consecutive cases of bacillary dysentery treated from 1930 to 1941 at the Gorgas Hospital, Panama Canal Zone. During this time all the cases were sporadic except for one major outbreak of 33 cases of Flexner type in an army post. This author observed a case fatality of 6.5 per cent. The use of polyvalent serum failed to reveal evidence that such therapy was of value. Flexner organisms were isolated from 91 per cent of the cases, and Sonne organisms from 6.5 per cent; no Shiga bacilli were obtained. The stools of 2206 food handlers were examined, and only 5 were found to harbor *Shigella* organisms—2 contained Flexner and 3 Sonne bacilli.

A considerable advance has been made in the laboratory diagnosis of this disease. Wheeler and Burgdorf⁹³ found that the determination of bacteriophage was of value as a supplemental procedure in institutional outbreaks, especially if laboratory examinations were not made until some time after the onset of symptoms.

The comparative efficiency of differential mediums has been studied by many. Mayfield and Gober,⁹⁹ of Mississippi, compared desoxycholate citrate, plain Endo, lithium chloride Endo and bismuth sulfite agars by culturing 435 stool specimens. The desoxycholate citrate medium isolated 95 per cent of the strains, a much higher efficiency than that of the other mediums. A comparison of the desoxycholate citrate and Difco S. S. (Shigella-Salmonella) agar with 1062 fecal specimens revealed that the latter was even more efficient.

Wilson and Blair¹⁰⁰ determined that a tellurite, iron and rosolic acid medium was selective for Flexner organisms; it inhibited bacilli of the coliaerogenes group, and the growth of Salmonella, typhoid bacilli and cholera vibrios was suppressed. Bradshaw¹⁰¹ compared Wilson-Blair medium with MacConkey plates and found the former preferable for Flexner organisms.

Pot¹⁰² compared Endo and S. S. agars for the isolation of Flexner, Sonne and Schmitz bacilli and obtained better results with the latter. Hardy, Watt and DeCapito¹⁰³ likewise found S. S. agar better than desoxycholate citrate agar. They describe a rectal-swab method for obtaining specimens in large institutions or for surveys. A dry swab is enclosed in a lubricated rubber tube and inserted past the anal sphincter. By withdrawing the tube 2 to 3 cm., the swab is left protruding. The applicator is then rotated with a sweeping motion and drawn back into the rubber tube. In this position it is removed and the specimen is plated. One precaution must be observed: the tube should be compressed between the fingers to prevent an undesired discharge of fecal material.

Numerous sporadic outbreaks of bacillary dysentery occur annually, and many find their way into the literature. It is not unlikely that this group of diseases will cause disability among the armed forces as they enter areas with primitive sanitation where the disease is relatively prevalent. Most of the references cited below have been selected because they illustrate the prevalence of Shigella infections in the United States.

Block and Ferguson¹⁰⁴ described an outbreak of dysentery in 1938 in Michigan. Several different types of Shigella, including Sonne and Hiss-Y bacilli, were isolated from 159 cases of diarrhea in a rural area. The source was not determined.

The predilection of Shigella infections for institutions and summer resorts is illustrated by the following outbreaks. The first, an institutional one in Connecticut, is described by Godfrey and Pond,¹⁰⁵ who traced the vehicle to ice contaminated by a woman handler who herself was ill with the disease. Ninety per cent of the physicians, nurses and waitresses were ill with Flexner dysentery. The ice was added to pitchers of drinking water in the doctors' and nurses' dining rooms. Quinlivan¹⁰⁶ describes an outbreak of Flexner dysentery in New York, causing 105 cases among 340 boys in a summer camp. The vehicle was raw milk infected by one or more milk handlers. Ingraham¹⁰⁷ describes two milk-borne epidemics traceable to a single dairy in a small village in rural New York. The first outbreak consisted of 134 cases of Flexner dysentery. Five months later, 73 cases of scarlet fever with 3 deaths were traced to the same dairy. After these two outbreaks the village finally passed an ordinance requiring the pasteurization of milk. Another institutional outbreak is described by Hardy et al.¹⁰⁸ There were 97 cases of bacillary dysentery due to the Newcastle bacillus, chiefly among nurses in a hospital in New York City. The organism was isolated from 76 of 97 cases. The vehicle was food prepared in the kitchen of the nurses' home, where it was contaminated by an undetected carrier. Felsen and Wolarsky¹⁰⁹ recommend a hospital epidemiologist, especially trained, preferably at the expense of the hospital, as highly effective in the control of bacillary dysentery. They map out a seven-point program, international in scope, for the control of the disease. Thorne and Estabrook¹¹⁰ report on an outbreak of Flexner dysentery, associated with infectious jaundice, in a state school in Vermont. There were 32 cases with dysentery alone, 26 with dysentery and jaundice and 62 with jaundice only. The jaundice occurred about one week after the dysentery. The outbreak was traced to a carrier in the kitchen as the probable source. Unclean clothing may also have been a factor in its spread. Flexner bacilli were isolated from 5 patients with dysentery only, from 2 with both dysentery and jaundice, and from 5 with jaundice only.

The possibility of war prisoners as foci of outbreaks is cited by two British sources. The first reports²¹ the isolation of Shigella from 4 Italian prisoners who had had no symptoms for three to fifteen months previously. The Emergency Public Health Laboratory Service¹¹¹ reported culturing 900 stools from 300 Italian prisoners. Some specimens were plated directly on MacConkey agar, whereas others were inoculated into tetrathionate broth and plated after eighteen hours. Fifty-one

prisoners were found to be infected with dysentery bacilli. The transportation of large numbers of men is a means of spreading a variety of diseases into areas where the disease does not exist. Apparently the British authorities are exercising precautions to limit the transportation of disease to a minimum.

The therapy of bacillary dysentery has undergone a great change in the past few years. Ouyang,⁹¹ of China, reviewing the cases at Peiping, says that he treated his patients with regulation of diet and increased fluid intake. Drug therapy did not seem important. This view, however, is at variance with that of most authors. In 1939, Lawrence¹¹² reported in vitro studies in which sulfathiazole was found to be the most effective of the sulfonamide drugs then available against the colon-typhoid-dysentery group of organisms. Below sulfathiazole in effectiveness were sulfapyridine, sulfamethylthiazole and sulfanilamide, in that order. Cooper and Keller,¹¹³ comparing the effectiveness of sulfathiazole, sulfapyridine, sulfamethylthiazole and sulfanilamide in protecting mice against fatal doses of *Shigella paradysenteriae* (Flexner), found sulfathiazole to be the most effective and sulfanilamide the least effective. Libby's¹¹⁴ work revealed that, in vitro, sulfathiazole is more effective against the Flexner bacillus than are the other sulfanilamide compounds. Taylor¹¹⁵ concluded that sulfathiazole is effective in the treatment of children with parenteral diarrhea or bacillary dysentery, particularly the latter. Good results in the sulfathiazole treatment of infectious diarrhea have been reported by other workers. Some of these studies, however, were inadequately controlled. Cooper and his associates¹¹⁶ report that sulfathiazole is of greater therapeutic value in patients whose stools are positive for dysentery organisms than in those whose stools are negative for these pathogens.

Hawking,¹¹⁷ in 1942, studied the concentrations of various sulfonamides in the feces of cats, mice and men. In cats, the highest concentration of all compounds was observed. In mice, sulfathiazole seemed more effective than sulfaguanidine in diminishing the number of bacteria, but the dosage required was toxic. In men, sulfaguanidine was found in the feces in high concentrations but sulfapyridine, sulfathiazole, sulfadiazine and sulfanilylbenzamide were found in fairly low concentrations. These experiments indicate that sulfaguanidine is the drug of choice for the treatment of bacillary dysentery.

Most authors write favorably of sulfaguanidine as shortening the clinical course of the disease, reducing the number of stools per day and helping to prevent the convalescent carrier stage. Lyons,¹¹⁸

of the United States Navy, treated 23 cases with sulfaguanidine and had 23 cases as controls. Five cases were not aided by the drug; 18, however, had striking benefits. There was a fall in temperature and leukocyte count in twenty-four to forty-eight hours, with concomitant reduction in the number of stools and clinical improvement. The drug was administered as a powder in milk—0.1 gm. per kilogram of body weight as the initial dose, followed by 0.05 gm. per kilogram every four hours until the number of stools was less than five per twenty-four hours. Thereafter, the dosage was reduced to 0.05 gm. per kilogram every eight hours for the next forty-eight to seventy-two hours.

Anderson, Cruickshank and Walker¹¹⁹ used sulfaguanidine in 41 adults who had Flexner dysentery with beneficial results, as compared with 55 controls. The dosage was 9 gm. per day in 3-gm. doses for two days, followed by 4 gm. per day in 2-gm. doses. If the diarrhea was not controlled in four days, a maintenance dose of 4 gm. per day was continued for a week. Such high dosages were beneficial and without toxic effects. Patients, however, must have a high fluid intake to prevent crystallization of the drug in the urine. Hardy, Watt, Peterson and Schlosser¹²⁰ are convinced that sulfaguanidine therapy is indicated for both cases and carriers. Their results were best with the Flexner and Newcastle varieties, where patients ceased to have *Shigella* in the stools by the tenth day, as compared with untreated cases where the organisms were isolated for two to three months. Their conclusion concerning the efficacy of the drug in the Sonne variety of dysentery is guarded, since these cases required a greater dosage over a longer period of time, and did not become negative so quickly as did those with the Flexner and Newcastle varieties.

Fairley and Boyd¹²¹ treated 371 cases of bacillary dysentery, 135 of which were caused by the Shiga bacillus in the Middle East. Of the 96 cases with complete records that were analyzed, the earlier the treatment with sulfaguanidine, the less damage was there to the colon and the quicker was the recovery. This chemotherapy was also effective against the Flexner, Schmitz and Sonne varieties, but no data are given. These authors report favorably on the use of specific antitoxin for the treatment of patients infected with the Shiga variety of dysentery bacillus. Felsen¹²² used human convalescent serum in the treatment of bacillary dysentery but thinks that this therapy must receive further evaluation. He describes clinical and experimental observations that indicate the existence of acquired immunity, and conducted active and passive immunization with vaccine and human convalescent serum.

Much research has been carried out on the possible toxic manifestation of *Shigella* infections.¹²³ Some authors believe that definite constitutional symptoms are produced by the action of soluble toxins circulating in the blood. However, no one has yet successfully applied this theory to the therapy of human dysentery. As a matter of fact, references cited above indicate that a polyvalent dysentery serum is not efficient as a therapeutic agent. Shiga antitoxin seems to be the only preparation that has proved of clinical value. Sulfaguanadine remains the therapy of choice.

Brucellosis

Undulant fever, which was once responsible for an epidemic of unknown fever among British soldiers on the island of Malta, was imported to the United States in 1905 with a shipment of goats from Malta. In 1911 it was recognized as endemic in Texas. Three varieties of *Brucella* are recognized; *Br. melitensis*, a caprine strain; *Br. abortus*, a bovine strain; and *Br. suis*, a porcine strain. Although these organisms can penetrate the unbroken skin, most infections are acquired through the digestive tract. The vehicle in most cases is raw milk. According to Ravenel,¹²⁴ the disease has been recognized in Canada since 1929. This author points to the rôle of milk-producing animals, in this case the cow, as a possible source of infection to man. He urges proper examination of cattle for Bang's disease and pasteurization of milk as protection against brucellosis and other animal diseases.

Huddleson's¹²⁵ *Brucellosis in Man and Animals* is a recognized work containing details on the epidemiology, pathology, clinical types, analysis of symptoms and treatment of this disease. He reviews 21 cases. Harris¹²⁶ devotes a major portion of his text to the symptomatology and diagnosis of clinical and subclinical infections. The prevalence, according to him, is wide. Eleven to 20 per cent of the cows in the United States are infected, and 20 per cent of the hogs in Iowa are victims of brucellosis.

The importance of brucellosis of cattle—Bang's disease or infectious abortion—was studied by Eichhorn and Crawford,¹²⁷ of the United States Department of Agriculture. They evaluate the various methods of controlling the disease in animals, such as the vaccination of cattle, the testing and slaughter of positive reactors, herd management, the testing and segregation of reactors and the prevention by proper examination of new additions to herds.

Simpson¹²⁸ gives an excellent description of the varied onsets and symptoms of brucellosis in man. "Many neurasthenics," he states, "whose chief

complaints were exhaustion, insomnia, irritability, and a variety of aches and pains have been found to be victims of chronic brucellosis." Clinical grounds for diagnosis are insufficient, since laboratory data must support the clinical picture. Like all the other authors who discuss this disease, he states that the best treatment is prophylaxis, namely pasteurization of milk.

The evaluation of therapeutic agents is still pending. Since the disease is greatly varied and is prone to improve or lapse spontaneously, more extensive and more accurate control data than those currently available are necessary before definite conclusions can be reached. Simpson does not encourage the use of sulfanilamide. Huddleson¹²⁵ and Harris¹²⁶ both advocate the use of vaccine or brucellergin for the treatment of chronic and selected cases. Harris believes that chemotherapy with sulfonamides may prove beneficial. Sarvis¹²⁹ treated 3 cases with sulfaguanidine with apparent cure. Caution, however, must be exercised in the evaluation of therapeutic procedures because of the protean nature of the disease and because of its tendencies to spontaneous remission or relapse. Certainly much further experimentation under properly controlled conditions is required before a final opinion on the efficacy of specific therapy or chemotherapy can be given.

Wood¹³⁰ points out that brucellosis is on the increase in the United States. All ages and both sexes are susceptible, the average incubation being fourteen days. He recognizes three types: pernicious, undulant and continuous. A positive agglutination test at a titer of 1:80 or higher is significant; however, it must be remembered that agglutinins may persist in the blood for four to ten years. A skin test with 0.05 cc. of a killed suspension of organisms injected intracutaneously or a 1:10,000 dilution of Huddleson's brucellergin gives induration as a positive response. Its interpretation, however, must be guarded.

Shronts¹³¹ cites four modes of infection: the ingestion of raw milk or raw-milk products, the handling of infected animal discharges or the carcasses of infected animals, the consumption of inadequately cooked meat of an infected animal and contact with brucellosis patients. The first mode is by far the most frequent; the last two are rare. Reinfection may be a factor in chronic brucellosis, states Manchester,¹³² who points out that often the disease is unrecognized and the patient continues to consume the *Brucella*-laden raw milk.

Foshay¹³³ evaluates the various laboratory aids to diagnosis. The clinician, however, must be aware of the protean aspects of the disease. In diagnosis, the clinical picture is the most important factor; laboratory procedures are secondary.

The most reliable procedure is the culture of the organism. The second most reliable aid is a high titer of agglutinins in the serum. It is well to remember that 6 to 10 per cent of culturally positive cases fail to develop agglutinins. The agglutination test, therefore, should not be used diagnostically to eliminate brucellosis. The intradermal or skin test is the third most useful one. It is performed with a killed suspension of organisms, a filtrate or a protein derivative. A positive skin test, however, does not necessarily indicate that the active disease is brucellosis; it means only that the patient has had contact with *Brucella*, either past or present. The skin test does not distinguish between past or present or latent and active disease. The patient may never have had a clinical case of brucellosis. An opsonocytophagic index may give aberrant results in some cases. Fluctuations occur rapidly in convalescent and recovered patients over short periods of time.

Fulton¹³⁴ describes how the prevalence of contagious abortion of cattle and undulant fever in man was reduced in Saskatchewan by requiring in certain districts the annual testing of dairy herds before milk was sold and by the education of stock owners in the desirability of having healthy, disease-free cattle. The 1933-1939 data gave 5.68 per cent of cows and 4.34 per cent of men as infected; in 1938-1939 only 4.34 per cent of cows and 2.11 per cent of men were infected. In Massachusetts, according to Rubenstein,¹³⁵ the situation is apparently reversed. There has been a gradual increase in the number of reported cases. This increase, however, is more apparent than real, and is explained in part by greater interest in this disease, and in part by better diagnostic laboratory aids. Feemster and Hyder¹³⁶ cite data showing that the number of cases in this state more than doubled from 1931-1935, when 98 were reported, to 1936-1940, when there were 227. Of 325 cases, 85 were in communities of over 25,000 population and 240 in communities of less than 25,000. Moreover, some of the patients in the larger communities were probably infected while on vacation or during visits to smaller communities where they consumed raw milk. The symptoms, in order of frequency, were fever, chills, sweats, weakness, headache and general aches. Of 337 patients, 212 (64 per cent) used only raw milk, 52 (15.4 per cent) both raw and pasteurized milk, and 32 (9 per cent) pasteurized milk. In 38 cases (11 per cent) no data on the milk supply were given. Of the 32 patients who claimed that their primary milk supply was pasteurized, 14 used raw milk from other sources. Eleven stated that they used only pasteurized milk: 2 of these had handled aborting cows, 3 handled carcasses of animals, 1

was an employee of a piggery where other cases occurred, 1 had no symptoms, 1 had a positive agglutination after a skin test had been performed, and in the remaining 3 there was suspicion that raw milk had been used. Of 7 patients using only pasteurized milk and no secondary supply, 3 were in contact with cows or pigs, 2 may have been infected from cheese, the diagnosis was questionable in 1 case, and the last patient probably used some raw milk.

The increase of undulant fever in Massachusetts occurred in spite of the fact that 90 per cent of the population in 1940 were using pasteurized milk. Feemster¹³ records two outbreaks of undulant fever, with 7 and 5 cases, respectively, between 1933 and 1940. In 1941, *Br. suis* was isolated from a raw milk supply in a central Massachusetts town.¹³⁷ This supply was responsible for 14 recognized cases of brucellosis—the largest single outbreak on record in Massachusetts.

An extensive outbreak of undulant fever due to *Br. suis* in Iowa in 1941 is described by Borts et al.¹³⁸ Seventy-seven cases were diagnosed as brucellosis on the basis of positive clinical or agglutination findings. *Br. suis* was isolated from the raw milk supply. These authors point out that blood culture stands first as a diagnostic aid in confirming the clinical diagnosis, especially when supplemented by the Huddleson dye methods whereby the species of the organism can be determined. The agglutination test, repeated when negative, is their second choice.

Br. melitensis has likewise been isolated from cow's milk. Duke¹³⁹ reports finding this variety in the milk from 3 of 76 cows in a herd that had been accredited for fourteen years, on a farm where goats had never been kept. Huddleson and Munger¹⁴⁰ describe an epidemic due to *Br. melitensis* among students who took courses in a laboratory building at Michigan State College. There were 45 clinical and 49 subclinical cases. The manner in which the students became infected is not described.

Menton¹⁴¹ isolated *Br. abortus* from 29 per cent of milk samples from cattle whose serums contained agglutinins and from 9 per cent of those that did not. This work illustrates the fact that the same phenomenon occurs in cattle as in human patients; namely, a certain percentage (9 per cent in cattle and 6 to 10 per cent in men) do not develop agglutinins in spite of the cultural demonstration of infection with *Brucella*.

Elkington et al.¹⁴² describe an extensive mild epidemic due to raw milk in a boys' school. There were 26 cases in a population of 400. *Br. abortus* was grown from the milk.

The literature on brucellosis is copious and cannot be reviewed. The outbreaks cited above are examples of the various phases of the disease that are likely to be encountered.

Mancera¹⁴³ describes the autopsy findings in a thirty-three-year-old woman who died of chronic brucellosis. Wechsler and Gustafson¹⁴⁴ give the history and autopsy findings in a twenty-eight-year-old farm hand. The characteristic post-mortem findings are generalized sepsis with abscess formation in the various viscera, especially the kidneys, and a positive culture from various parts of the body.

Wise and Poston¹⁴⁵ cultured 14 consecutive cases of Hodgkin's disease and isolated *Brucella* in all. When 67 patients from the same area with lymphosarcoma, leukemia or tuberculous adenitis were cultured, no positive results were obtained, with one exception. There seemed to be some correlation between the *Brucella* infection and the clinical course. However, many more data are necessary before one can assume that the *Brucella* organisms are the etiologic agents of the clinical manifestations of Hodgkin's disease.

Streptococcal Infections

The usual vehicle for food-borne hemolytic streptococci is raw milk. Dublin, Rogers, Perkins and Graves¹² studied milk-borne outbreaks in upstate New York from 1917 to 1941. During these twenty-four years there were 168 outbreaks, with 9989 cases; 57 (34 per cent) of the outbreaks, which involved 6812 (68 per cent) of the cases, were due to streptococci causing septic sore throat and scarlet fever. All of them were due to raw milk except one, where improperly pasteurized milk was incriminated. These authors typed the streptococci responsible for recent milk-borne outbreaks and cite data for 6 foreign outbreaks of a similar nature. From 1935 to 1942, there were 9 outbreaks in upstate New York due to hemolytic streptococci. One of these, with 44 cases of scarlet fever due to a Type 3, Group A, streptococcus, was traced to an infected cow's udder.¹⁴⁶ The raw milk was secured at a local cheese factory where the milk of 6069 cows was pooled. The cow responsible for the outbreak was located by a Breed smear and a bacteriologic follow-up of the suspected herds. The cow had suffered a teat injury that was later infected through manipulation by a person with a sore throat.

In April, 1942, 6 cases of scarlet fever and 24 of septic sore throat were traced to raw milk coming from a Cheddar cheese plant in a small community in Delaware County, New York.¹⁴⁷ Epidemiologic evidence suggests that the ultimate

source of contamination was one of the numerous producers who brought to the plant 150,000 pounds of milk daily.

Feemster¹³ reviewed milk-borne disease in Massachusetts from 1933 to 1940. Of the 6 outbreaks, with 469 cases, 4 consisted of scarlet fever or sore throat and were responsible for 412 cases.

In July, 1941, a ham borne streptococcal outbreak occurred in a small town in Massachusetts.¹³⁷ One of two hams was infected by a woman who was in the pre-eruptive stage of scarlet fever. The hams were ground and the meat made into sandwiches, which were left standing at room temperature for twenty-four hours on a hot summer day and then served to 200 people. As a result, there were 24 cases of scarlet fever, 56 cases of septic sore throat, 7 of diarrhea, 7 of nausea and vomiting and 8 of miscellaneous complaints. Gastrointestinal symptoms were unusually prominent in all the patients. A hemolytic streptococcus (Type 2, Group A) was isolated from the throat of the responsible food handler, from the ground ham and from the throats of several patients. Animal experimentation and other laboratory procedures suggest that an enterotoxin substance not dissimilar to staphylococcal enterotoxin may have been responsible for the unusually large incidence of nausea, vomiting and diarrhea.

Bloomfield and Rantz¹⁴⁸ report an outbreak of streptococcal septic sore throat and scarlet fever transmitted by food other than milk in a western United States Army camp. There were 341 cases in one of the units. About one fourth of these patients developed a typical scarlet-fever rash. The streptococcus was Type 15, Group A. There were no fatalities, and complications such as peritonsillar abscess and otitis media were uncommon.

(To be concluded)

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29241

PRESENTATION OF CASE

A forty-two-year-old man, a hairdresser, entered the hospital because of crampy abdominal distress, associated with bouts of diarrhea.

Approximately three years prior to admission the patient began to have brief attacks of sharp gripping pain in the right lower quadrant that disappeared with massage. Five months prior to admission he developed an aching pain in the right hypogastrium that radiated to the epigastrium and to both flanks, not associated with nausea or vomiting. Several times a day he had intermittent brief periods of tenesmus that were usually relieved by bowel movements. The stools were watery and "clay colored" but were not tarry or bloody and did not contain mucus. Four months prior to admission the cramps occurred almost constantly and the stools remained light in color. One month prior to admission he had to give up work because of the abdominal cramps and diarrhea. A barium meal at that time outlined a normal esophagus and stomach. The duodenal bulb filled and showed a deformity with a small ulcer crater on the lesser curvature. The remainder of the duodenum and upper jejunum were not unusual. The head of the motor meal was in the hepatic flexure. Despite an ulcer regime and the administration of tincture of belladonna the abdominal difficulty persisted, and two weeks prior to admission the crampy abdominal pain was localized in the right lower quadrant of the abdomen. During the illness he had lost 20 pounds.

The family history was not remarkable. Thirty years prior to admission the patient had had typhoid fever, from which he recovered without sequelae. Fifteen years prior to admission he developed a pleural effusion associated with severe, sudden pain in the left chest and shoulder, which was worse on deep inspiration and coughing. There were no chills, fever, cough or bloody sputum. Bloody fluid having a specific gravity of 1.040 was recovered, but repeated attempts to identify an infectious agent were unsuccessful both by culture and guinea-pig inoculations. X-ray films of the chest after removal of the pleural fluid

were not remarkable. After a month of hospitalization the patient was discharged on limited activity and subsequently gained weight and felt well.

Physical examination disclosed a thin but well-developed man in no apparent discomfort. A 2-by-4-cm. tender, fixed mass was felt in the right lower quadrant of the abdomen. Breath sounds were diminished at the left apex posteriorly, and occasional coarse rales were audible in this area. The heart was normal. The prostate was slightly enlarged and tender.

The blood pressure was 120 systolic, 80 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 5,010,000, with a hemoglobin of 13.6 gm., and a white-cell count of 13,000 with 72 per cent neutrophils. The urine was normal. The stool was light brown, watery and guaiac negative. A blood Hinton test was negative. Sputum examination was negative.

An x-ray film of the chest showed considerable scarring in the right supraclavicular and infraclavicular areas, in which were observed round areas of decreased density suggestive of small cavities, in several of which there were fluid levels. The lower right lung field appeared slightly emphysematous. The heart was not remarkable.

A barium enema demonstrated spasm of the cecum. The cecum filled with some difficulty and showed an irregularity of its lower edge that could be made to disappear with pressure. The organ was mobile. There was reflux into the terminal ileum, but this did not fill in the usual way and seemed somewhat adherent to the cecum. A small-bowel enema employing 1000 cc. of diluted barium appeared in the colon in eight minutes, and the patient was not uncomfortable throughout the examination. The folds in the distal ileum were slightly wider than usual, but there was no rigidity of the wall. By palpation, barium could be ejected through the ileocecal valve into the colon; the ileum was seen to balloon out during this procedure. There was a markedly irregular narrowing of the lower portion of the ascending colon immediately above the ileocecal valve. The rigidity extended downward and involved the upper 2 cm. of the cecum. The cecum below was distensible but showed some swelling of its mucosal folds. The appendix was markedly dilated. The ileocecal valve was rigid but not narrowed.

An operation was performed on the twenty-ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. CLIFFORD C. FRANSEEN: This is the familiar problem of differential diagnosis of

*On leave of absence.

sociated with the cecum, and here, as in most of these cases, much depends on accurate observation on the part of the roentgenologist. Let us review the possibilities and probabilities of what one might expect to find before we look at x-ray films. We know that this patient's history was a relatively long one. If we assume that all the symptoms were related to the present illness they go back three years, which is a little long for a malignant tumor. He did have a small duodenal ulcer, and it is true that he had lost 20 pounds in weight. In spite of this loss in weight, there was no anemia. He showed some irritability of the small bowel, since a small bowel enema went through in eight minutes. Is that not quite rapid, Dr. Robbins?

DR. LAURENCE L. ROBBINS: From seven to fifteen minutes is usually considered to be within normal limits.

DR. FRANSEEN: Another important observation is that the stool was guaiac negative. Other important findings in the history are pleural effusion, typhoid fever, a fixed tender mass in the right lower quadrant, and signs at the apices of the lungs. Most of the other things depend on the x-ray findings, and certainly from their description I should interpret all of them as being suggestive of some inflammatory lesion. We will now look at the films, if we may.

DR. ROBBINS: The film of the chest shows evidence of tuberculosis at the right apex, and this film shows the duodenal ulcer. The lesion in which we are chiefly interested is this one in the proximal colon. It was not well visualized at the time of the barium enema, but there is more evidence of spasm than there is of actual rigidity. In the films following the small-bowel enema, there is a particularly good demonstration of the ileocecal valve. It appears to be about normal in diameter, but it changes perhaps a little bit, and there is the appearance of the rigidity along this margin.

DR. FRANSEEN: Only the upper 2 cm. of the cecum and the ileum are involved by adherence?

DR. ROBBINS: Yes.

DR. FRANSEEN: The report says that there were cavities in the chest showing fluid levels.

DR. ROBBINS: I am not sure that I can see any fluid levels. In fact I am not positive that there is definite evidence of activity from the x-ray findings alone.

DR. FRANSEEN: The sputum was negative.

DR. ROBBINS: There is certainly evidence of old tuberculosis.

DR. FRANSEEN: First in the differential diagnosis we ought to consider inflammatory lesions of the cecal region. Appendiceal abscess is always

foremost. We know it can simulate any of these masses in the right lower quadrant. I remember distinctly two patients I saw a few years ago, one a relatively young man and the other an old man, both with masses in the cecum. For both, a right colectomy was done. The young man turned out to have carcinoma, and the old man an appendiceal abscess. That is the way we are often misled by these lesions. Of course, with a history of this type it would be unlikely for the lesion to be an appendiceal abscess. These symptoms suggest that the patient had intermittent bouts of obstruction over a relatively long period of time. The next numerically important inflammatory mass in the region of the cecum is tuberculosis. When Adams and Parsons¹ looked up the cases of tuberculosis of the cecum here a couple of years ago they found 38 over a period of fifteen years, which means a little better than 2 cases a year in this hospital. I am not sure that we have that many cases of regional ileitis with masses in the right lower quadrant; hence, numerically, perhaps tuberculosis is next in order.

What are the possibilities that this was tuberculosis? There had been or was tuberculosis at the apices of the lung, and the description of the lesion in the cecum is entirely consistent with tuberculosis. To have the two findings together is more suggestive than the lesion in the cecum alone. In Adams and Parsons's series they found that approximately half the patients who had tuberculosis of the cecum had no signs in the lung, either by physical examination or by x-ray. I am sure that many of us before that time believed from our teaching that it was almost invariably associated with advanced pulmonary tuberculosis.

In spite of the fact that the patient had evidence of tuberculosis in the apex of the lung, a dual diagnosis must be seriously considered, which one is always loath to do. What else can it be? From the description of the mass and from the patient's symptoms and the physical and x-ray findings one cannot exclude an area of regional enteritis, but it seems less likely than tuberculosis with the evidence at hand. Actinomycosis and other similar infections have to be considered as well. But I do not believe that Dr. Robbins would suggest that there was much possibility that this lesion in the lung was actinomycotic, and over this period of time the patient would have had other constitutional symptoms from this disease.

A foreign body with inflammatory tissue around it must always be considered in the peritoneal cavity, but so far as we know the patient had not had a previous abdominal operation at which one might have been introduced.

One should always consider possibilities of tumor, but I admittedly am not considering them

so seriously as an inflammatory lesion. The history is too long for carcinoma, and the x-ray findings are not compatible with it. Tumors such as we find in this region, particularly lymphomas, carcinoids of the appendix and terminal ileum and other tumors of the terminal ileum that may in

with fixative before opening so that the relation of the lesion to the bowel lumen could be better demonstrated. When sectioned (Fig 1), a firm grayish white inflammatory mass involving the ascending colon, ileocecal valve and a portion of the cecum was seen. There was also some in



FIGURE 1 Hyperplastic Tuberculosis Involving the Ileocecal Region

volve the cecum, all seem to be fairly well ruled out by the x-ray evidence. So when we consider all these things together it seems to me it would not be fair to make any other diagnosis than that of tuberculosis.

CLINICAL DIAGNOSIS

Tuberculosis of cecum

DR FRANKS'S DIAGNOSIS

Tuberculosis of cecum

ANATOMICAL DIAGNOSIS

Tuberculosis of cecum

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN: The ascending colon, cecum, appendix and a portion of the terminal ileum were resected. On the serosa there were a few grayish, granular, 1 mm nodules that suggested tubercles. The pericolic fat was porky and adherent to the bowel. The specimen was injected

with this degree of stenosis, it is surprising that there was not more evidence of intestinal obstruction. The regional nodes were caseous, and the wall of the appendix was hypertrophied. Microscopically the lesions proved to be tuberculous.

This makes the third surgical specimen of tuberculosis of the cecum that we have had within a period of four or five months—a much higher incidence than we usually have. These three cases belong to the so-called hyperplastic type of tuberculosis, which produces stenosis rather than ulceration, although all three lesions showed some degree of ulceration. The pure ulcerative type is almost always associated with active pulmonary disease.

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CASE 29242

PRESENTATION OF CASE

A sixty-five-year-old Greek shoemaker entered the hospital complaining of hematuria.

Ten years before admission the patient noticed that he frequently passed small amounts of blood in his urine at the end of urination (terminal hematuria). There was no pain or dysuria but

was found to give a $++$ test for albumin; the sediment contained 40 to 50 red and white cells per high-power field. Cystoscopy showed a slightly inflamed bladder, and an intravenous pyelogram was reported as negative. A mass was palpated in the right upper quadrant. The patient had been otherwise well and had not lost any weight.

Physical examination showed a well-developed and well-nourished man. Examination of the

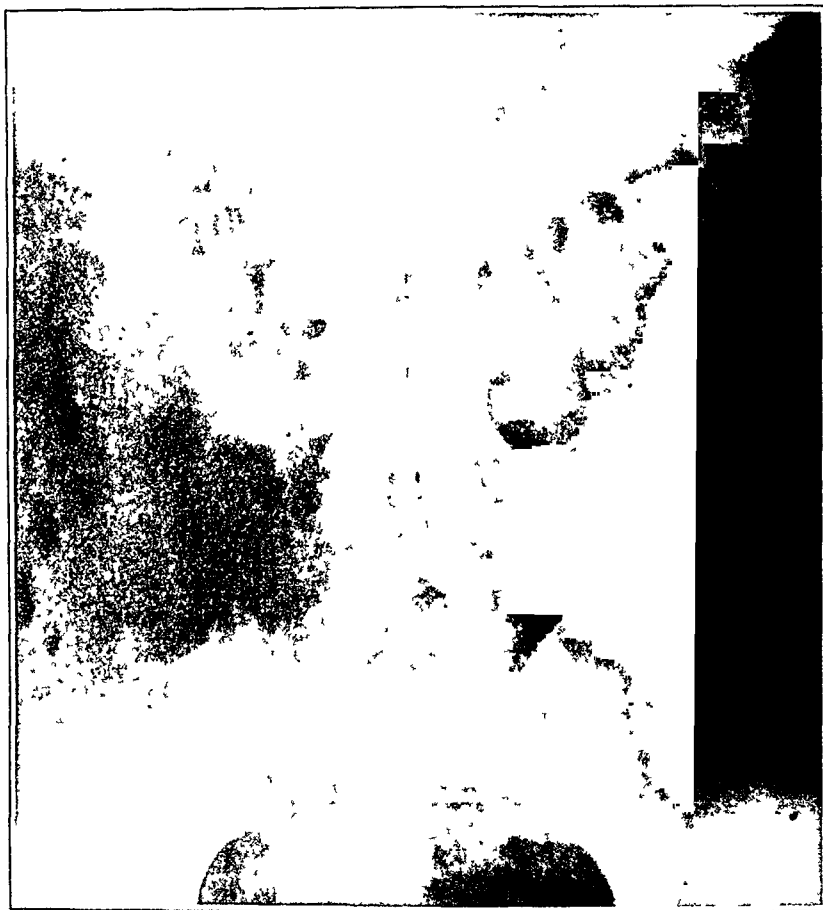


FIGURE 1. *Retrograde Pyelogram Showing a Mass in the Region of the Middle Calyces.*

there was some frequency. He was studied at a community hospital for three weeks, but no definite diagnosis was reached. The situation continued unchanged until five years before admission when gross hematuria suddenly occurred, lasting several days. At the same time he had sharp twinges of pain in the right upper quadrant, which was related only to changes in posture. He was again hospitalized and treated symptomatically. Meanwhile other urinary symptoms had developed gradually — day and night frequency, poor stream and incontinence. All had persisted, although the hematuria had been intermittent, and at times a few small black clots were passed at the end of urination. Five months before entry he was seen in the Out Patient Department, where his urine

heart and lungs was negative. When lying on his left side, a firm, smooth, ovoid mass about the size of an orange was felt just below the right costal margin. This mass moved with respiration, was moderately tender and disappeared upward and posteriorly as the patient was slowly turned on his back.

An intravenous pyelogram showed prompt excretion of the dye on both sides. The right upper calyces were slightly separated from each other. These findings were confirmed by a retrograde pyelogram, which showed a mass 3 or 4 cm. in diameter in the region of the middle calyces (Fig. 1). No protrusion could be seen on the outside of the kidney.

An operation was performed on the eighth day.

DIFFERENTIAL DIAGNOSIS

DR. J. DELLINGER BARNEY: This man entered complaining of hematuria. The terminal hematuria ten years previously was apparently not definite, but suggests a lesion in the bladder or prostate. It was more or less an asymptomatic hematuria. The fact that the hematuria had gone on for five years and that the man was, as stated later in the history, well developed and nourished indicates that the lesion, if a tumor, was not increasing rapidly in size and had not metastasized. The pain in the right upper quadrant may have had nothing to do with the kidney, that is, may have been muscular or arthritic pain.

The frequency of urination, both day and night, brings up the question of an inflammatory process either in the bladder or in the kidney. It does not suggest a prostatic condition, in which there may be night frequency, but usually none during the day unless there is considerable infection. We often speak of patients having incontinence when they have nothing more than marked urgency. Hematuria followed by clear urine for a few days is not at all unusual with renal lesions. A cystoscopy was done, — and properly, — which showed only a slightly inflamed bladder and thus ruled out stones and tumor of the bladder and prostatic trouble.

The palpation of the mass in the right upper quadrant more or less focuses our attention on the kidney, although it might have been something else. In this case I shall say that it was kidney. It might have been a tumor or a cyst. The fact that the patient had not lost weight for ten years suggests that he did not have malignant disease, although some patients may have a tumor of the kidney for at least ten years without showing any loss of weight or strength. The deformity of the calyces, together with the mass in the region of the middle calyx, with no protrusion outside the kidney, indicates that the mass was inflammatory, or if malignant, was some intrarenal mass that did not involve the calyx but did involve the pelvis. In other words we might be dealing with a pelvic tumor with encroachment on the calyces.

In view of the story and the apparently negative cystoscopic examination I believe we are forced to come down to the right kidney as the source of this man's trouble. One can think of a great many things that would cause hematuria, and as I have indicated, there are many things that can cause a palpable mass in the right upper quadrant, some of which can be mentioned but ruled out — tuberculosis, for instance. Although such a lesion might have persisted for ten years, the patient was a little old for renal tuberculosis, and

he did not have the bladder symptoms that one usually finds with this disease. A stone in the kidney might also have caused hematuria and enlargement of the kidney, but in all these years I think it would have produced more pain at one time or another. In view of the x-ray evidence, he apparently did not have a stone. He might have had a cyst — one of those so-called "solitary cysts" of the kidney, which may go on for a long period of time, causing hematuria and, in certain cases, presenting a mass such as the one palpated in this case, but without producing any constitutional disturbance.

We might mention a carbuncle in the kidney, but it is unlikely that the patient would have had a carbuncle for ten years without acute pain or tenderness. Since this man was a Greek, we might think of echinococcal cyst of the kidney, but I doubt that he would have had it for ten years without further trouble; I mention it for what it is worth. He may have had a hemorrhagic infarct of the kidney that was mistaken for a tumor in the pyelogram. This is also unlikely because in those cases that I have seen the onset has been sudden, and the duration brief. The x-ray findings rule out ureteral tumor.

The retrograde pyelogram shows wide separation of the upper and lower borders of the calyces and pelvis so that one can probably say that there was a mass. The outline of the kidney can be seen, and there is no evidence of a bulge.

DR. GEORGE W. HOLMES: I should like to help you, if I can. The kidney outlines are sufficiently visible so that one can say that there is not much difference in the size of the kidneys. That may be of some value. Here is the shadow of the deformity. I agree that it is distinct and definite. It is seen well in all the films, and I do not believe that it has changed appreciably in size during this period of time. That is consistent with a slowly developing mass, such as is indicated by the history.

X-ray examination of the bladder is notoriously inaccurate. There is a fairly normal bladder shadow. The question of the preparation of the patient before x-ray examination of the bladder is frequently brought up and warrants a statement. We can try to clean these people out, or take them as they are. If we give them a physic, they are apt to have a lot of gas, which may be a bother. If we give an ordinary enema, part of it is always retained and that obscures the findings. So usually we prefer to x-ray the patient as he is, unless he is known to be constipated, in which case the patient ought to be cleaned out a day or two in advance. As a rule, preparation does not help

a great deal, and I do not believe that it would have helped in this case.

DR. BARNEY: It seems to me that this case was one of an intrarenal, perhaps an intrapelvic, neoplasm of the kidney. It might have been an adenocarcinoma, such as one I saw once about the size of a golf ball that was entirely intrarenal and had existed for ten years; there possibly was some calcification, which might have produced secondary infection of the kidney. This was apparently not severe, since the patient had only relatively few white cells in the urine and no fever.

Is there any note about a culture?

DR. BENJAMIN CASTLEMAN: The culture showed a few colonies of *Staphylococcus albus*.

DR. BARNEY: That does not help us much.

I shall say that this was an intrarenal neoplasm of the kidney, probably an adenocarcinoma.

CLINICAL DIAGNOSES

Malignant tumor of kidney.
Prostatic hyperplasia.

DR. BARNEY'S DIAGNOSIS

Intrarenal neoplasm of kidney (adenocarcinoma).

ANATOMICAL DIAGNOSES

Cortical cyst of kidney.
Prostatic hyperplasia.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This patient was operated on by Dr. Colby, who removed the kidney. When it was sectioned we found a cyst measuring 3 cm. in diameter within the cortex of the kidney. It

did not produce a change in the external configuration of the kidney, thus confirming the x-ray findings. The cyst was thin walled, smooth lined and perfectly benign. Although most of the cortical cysts that we see extend out from the surface of the kidney, this one was completely intrarenal.

DR. GEORGE G. SMITH: Was there any explanation of the primary terminal hematuria?

DR. CASTLEMAN: The patient did well post-operatively, went home and then came back to the hospital because of persistent hematuria. Perhaps Dr. Colby will tell us the rest of the story.

DR. FLETCHER H. COLBY: This man had an enlarged prostate, and part of the bleeding came from there. However, when he was investigated thoroughly, we found this deformity of the kidney. We thought it was significant enough to operate on him to find out whether it was a benign or malignant tumor. Our diagnosis before operation was malignant tumor of the kidney. The kidney was exposed through a transperitoneal approach. When the kidney was thoroughly exposed we could see nothing on the surface to suggest tumor. When the kidney was felt between the two hands, in the middle portion a thick, hard area could be palpated, so the kidney was removed. We did not know until after it had been removed that this was a cyst rather than a tumor. The patient before he left the hospital again had gross hematuria, which was obviously from the prostate. We eventually did a transurethral resection of the prostate.

DR. BARNEY: This is an extremely interesting case. In my experience an intrarenal solitary cyst is rare. I had one almost identical with this a great many years ago.

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WAR, HOSPITALS AND NURSES

ABOUT 274,000 graduate nurses are available in the United States. The Army and Navy expect to enroll 60,000, or 22 per cent of all nurses, by the end of 1943. It is estimated that the hospitals of this country need 223,000 nurses and that 67,000 more are required for private duty, public health and industry. Hence, the total number of nurses necessary to meet all demands is 350,000, leaving a deficit of 76,000. It is apparent then that there are not enough nurses to supply both military and civilian demands. Military needs must be met. What can be done about civilian needs?

Part of the deficiency can be met through an increase of student nurses. On the basis that three students can do the work of two graduates this means 114,000 students. By November, 51,000 students will remain in nursing schools, so that between now and then 63,000 new students must be enrolled, and to assure this number, 84,000 young women must be examined.

The shortage of nurses in hospitals can also be helped through the use of accessory workers, such as ward helpers, extra maids and ward secretaries, who can do much of the nonprofessional ward work, thus releasing nurses for the more important nursing service. Volunteers have been found extremely helpful, especially Red Cross nursing aides and men from colleges and from business groups who fill in for the now almost nonexistent orderly.

Whence have Army nurses come to date and where will they be recruited in the future? Judging from the experience of the Massachusetts General Hospital, hospitals have provided a high percentage. There, the ordinary complement of graduate nurses is approximately 300, it is now less than 200. In other words, 33 per cent have gone, mostly into the armed forces—a figure that is 11 per cent higher than the average requirement. It is impossible to say whether this percentage is applicable to other hospitals, but it probably is typical of most teaching hospitals. Since hospitals obviously cannot afford to supply more nurses for military needs, whence can they come?

The special-duty group immediately comes to mind as a possible source. Most nurses of this sort are concentrated in cities, especially the large ones. Many of them, by reason of age, physique or family responsibilities, cannot assume institutional nursing but are able to work for short periods. Others prefer private duty. The last group is the only one immediately available both for Army recruiting and for replacing institutional nurses who have entered or are about to enter military service. To release them, it seems wise to reduce private duty to a minimum, supplying it only when required by serious medical needs of patients. Such a limit

tation can only be achieved by a determined co-operative effort by hospitals, physicians and patients. To this end some hospitals have already ruled that special nurses will be provided only on the request of the physician in charge, and it is hoped that this practice will be adopted by all hospitals. Although the number of nurses released in this way will not be sufficient to meet either the military needs or the necessary replacements in hospitals, it will help.

What else can be done to make up for the shortage in hospitals? Some relief will be forthcoming from married nurses who can arrange their family responsibilities in such a way as to allow part-time service in hospitals. Although some may consider themselves rusty, basic procedures do not change, and refresher courses and daily contacts with hospital routines will soon dispel their diffidence. Perhaps American hospitals may soon follow the example of England and Russia, which have established day nurseries for the children of working nurses.

The nursing shortage can also be helped by the reduction of nursing procedures ordered by doctors. Frequent taking and charting of temperature, pulse and respiration, blood-pressure recordings, hot packs, back rubs and so forth may be desirable under normal conditions but can be cut down without serious consequences. Medication, particularly intravenous therapy, can probably be advantageously reduced, and laboratory examinations requiring the collection of specimens by nurses and technicians should be requested only when there is valid medical justification. Furthermore, nursing procedures should be reviewed by the nursing-practice committee of the faculty of the school of nursing to simplify methods so that they will consume the least time that is necessary for effective and safe nursing care. And finally, patients should be encouraged to do many things that formerly have been done for them—carrying trays, obtaining water and helping to tidy the ward or room; they should also assist in keeping flowers, visitors and telephone messages at a minimum.

The continued operation of hospitals depends on the simultaneous operation of these and other makeshifts and the acceptance of these changes in the accustomed way of doing things by all concerned. Unless such adjustments can be carried out, two undesirable alternatives remain—a closing of hospital wards or floors at a time when the community demand for hospital care is greater than ever or a dangerous lowering of standards and methods of care because there are not enough trained nurses to care for patients or to superintend the work of untrained assistants. If physicians, nurses, patients and hospital can pull together, it can be done.

REHABILITATION OF THE DISABLED

ONE of the inaugural ceremonies of the opening of the Second War Loan was, fittingly enough, a broadcast by a one-legged soldier. He had not long been one-legged,—only since a short time after the memorable landing on an African beach,—but there was no question of his being irrevocably one-legged for life thereafter. One of the inescapable accompaniments of war has always been a slowly deteriorating army of physical and mental cripples, for whom some more or less adequate permanent provision has to be made, regardless of whether the bitterness of defeat or the sweets of victory have been tasted.

England, according to a leading article in the March 13 issue of the *British Medical Journal*, has been thinking seriously of rehabilitation as a duty of social medicine. In the 'Beveridge Report' it was described as a new field of medical activity, which of course it is not, since it has been practiced for years, but it is fair to say that new significance has been attached to it.

This necessity for rescuing and reconditioning and fitting back into useful activity of as many as possible of war's derelicts has been increased in England by the grim fury of total war, with the crippling of civilian populations and the ravaging

by disease that are left in its wake. Human rehabilitation or reconditioning is designated and is accepted largely as a sociomedical problem—that of carrying on with the patient beyond convalescence and to the point where his permanently reconstructed life begins. It means psychologic as well as physical rehabilitation, the finding or the making of many-shaped holes into which to fit many-shaped pegs, in addition to the safeguarding of the social readjustments of war's victims.

While the war is still going on, the problem is not so difficult as it will become later. The majority of able-bodied young men are in the services, the wheels of industry are turning busily, even if they are turning out only the engines of destruction, and there is a place for anyone who can do any kind of job. It is when the armies are demobilized and a host of healthy job hunters are turned back into civilian life, and when the machines that had made rifles and tanks and hand grenades come to a stop before finding new and more productive outlets, that the handicapped worker must be protected against competition that is too one-sided.

England's Interdepartmental Committee on Rehabilitation wisely refuses to accept the idea of granting subsidies to employers for hiring disabled men; it does approve the alternative of a statutory obligation on employers to accept a quota of reconditioned workers, with the setting up of a register of handicapped persons and a schedule of occupations that will be primarily reserved for them.

We, too, must be thinking along these lines, for our one-legged soldier of the broadcast is a symbol of the direction in which the path of glory leads. May the years following this war see fewer crippled veterans selling the poppies of forgetfulness at the crossroads.

MEDICAL EPONYM

WEIL'S DISEASE

This was first described by A. Weil (1848-1916), of Heidelberg, in an article entitled "Ueber eine

eigenthümliche, mit Milztumor, Icterus und Nephritis einhergehende, acute Infectiouskrankheit [A Peculiar Acute Infectious Disease accompanied by Enlargement of the Spleen, Jaundice and Nephritis]" in *Deutsches Archiv für klinische Medicin* (39: 209-232, 1886). A portion of the translation follows:

In all four cases we were dealing with an acute febrile disease that was accompanied by severe nervous phenomena with enlargement of the spleen and liver, icterus and nephritic symptoms, but which, after a relatively short duration of the severe symptoms, followed a rapidly favorable course.

R. W. B.

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COMMITTEE ON MATERNAL WELFARE

NEONATAL CASE HISTORY: BLEEDING INTO THE CEREBROSPINAL FLUID

E. H. was the second child of healthy parents and was born at term by normal vertex delivery. At birth he weighed 6 pounds, 4 ounces, and seemed normal. Vitamin K was administered by the obstetrician.

Seven hours after delivery the baby suddenly collapsed, with pallor, listlessness, cyanotic hands and feet, and a temperature of 93.4°F. He was placed in a Hess bed and allowed to warm up gradually. During the next three days he improved; although he was never alert, he took feedings well. On the fifth day he became jaundiced, refused his feedings and weighed 5 pounds, 6 ounces. The following day he vomited projectily three times and had obvious vigorous epigastric peristalsis. He had small fecal stools. Atropine given before feedings did not influence the vomiting. On the seventh day a gastrointestinal x-ray series showed a normal stomach and intestinal tract. On that day the fontanelle was noted to be tenser than formerly, and a lumbar puncture produced 20 cc. of port-wine-colored spinal fluid with a total protein of 1500 mg. per 100 cc. and a red-cell count of 1,200,000. The fontanelle remained soft for only a few hours, when it was again tense and bulging. Trouble was experienced in doing another lumbar puncture and resort was had to a cisternal tap, from which 30 cc. of entirely similar fluid was obtained. No fluid was obtained by puncture at the angles of the fontanelle. Following this, cisternal taps were performed twice daily for five days, with the removal each time of between 30 and 50 cc. of fluid. The circumference of the head diminished 19 mm. as a result of sev-

eral of the taps, only to return to its former size in ten or twelve hours. When the baby was thirteen days old the fluid reaccumulated less rapidly, and he was tapped daily until he was twenty-four days old and twice during the next ten days. Altogether twenty-four cisternal taps were made. The fluid gradually changed from wine red to brown, to yellow and, finally, to water clear, and the total protein at the last tap was 74 mg. per 100 cc.

An encephalogram was performed on the twenty-fourth day by the introduction of 10 cc. of air into the cisternal needle. The films showed moderate symmetrical dilatation of the lateral and third ventricles.

During the first two weeks the baby showed little interest in life but took his feedings tolerably well from a nipple. After that he ate well and became increasingly alert. He sat alone at ten months, stood in his crib at one year and walked at eighteen months; at two years he was speaking in short sentences, looking at picture books with interest and talking about the pictures, stringing large wooden beads on a shoestring and building with large wooden blocks. He was not toilet trained. An internal strabismus of the left eye had persisted since his acute illness.

Comment. The initial collapse of this baby seemed at first to be explained by excessive cooling, since he improved as his temperature reached normal. Vomiting and visible gastric peristalsis diverted attention to the gastrointestinal tract, but careful observation failed to show any structural abnormality. Finally on the seventh day of life the blood in the cerebrospinal fluid had so interfered with its absorption that hydrocephalus became manifest. In this connection it should be noted that a number of infants with hydrocephalus have been seen since this infant was observed who had been operated on in the first few weeks of their lives for what was thought to have been hypertrophic pyloric stenosis. Presumably the vomiting and increased peristalsis in these cases were the result of blood in the third ventricle.

The location of the hemorrhage remained in doubt; it may well have been intraventricular, since so much blood was so evenly distributed through the spinal fluid. An angiomatic tumor might well have been a source, but no lesion of this type was demonstrated by encephalography.

Grossly bloody spinal fluid is in itself damaging to the growing brain. Bagley* showed that amounts of a puppy's own blood as small as 2.5 cc. introduced into the cistern may produce hydrocephalus, meningeal thickening and microscopic changes in the cerebral structure, apparently be-

cause of interference with the apparatus for the absorption of spinal fluid. For this reason it was determined, in this case, to remove the blood as quickly as possible in order to prevent the development of hydrocephalus, if possible. Repeated cisternal puncture seemed to offer the safest means to this end, and by its use, large volumes of fluid were removed frequently enough to prevent excessive intracranial pressure. The elastic head of infancy made such a procedure feasible. As the fluid became less bloody, it reaccumulated less and less rapidly, and finally not at all. At two years of age the patient is a healthy boy with an internal strabismus.

WAR ACTIVITIES

INDUSTRIAL HEALTH

POISONING FROM NITROGEN OXIDES

As a result of the conference of medical directors from ordnance establishments where the hazards of poisoning from nitrogen oxides exists, held at Cincinnati, on January 28, the Office of the Chief of Ordnance has issued Industrial Hygiene Information Circular No. 11: "Nitrogen Oxides Poisoning." A consensus on the etiology, symptoms, prevention and treatment of poisoning from the oxides of nitrogen is presented. The following directives are given for the treatment of cases with significant exposure:

(1) Prevention of exposure is most important. It should be accomplished through proper engineering control and through safety education.

(2) Keep the patient warm and at absolute bed rest at least twenty-four hours. Disturb him as little as possible.

(3) Obtain a careful history and attempt to evaluate the exposure. Lean over backward in case of doubt.

(4) Obtain frequent recordings of pulse and respiratory rates and of blood pressure, and periodic blood counts and hemoglobin determinations.

(5) Venesection (300 to 600 cc.) may be indicated if pulmonary edema develops, unless the patient is in shock.

(6) Blood plasma may be of value to combat hemocentration.

(7) Continuous oxygen therapy, preferably by mask, catheter or tent, should be given. The use of slight positive pressure (1 to 6 cm. of water) by mask during exhalation may be useful.

(8) Prescribe a liquid diet, as tolerated.

(9) Keep sedation at a minimum because of the depressant action on respiration. Morphine is dangerous and should not be used.

(10) Complete and permanent records must be kept of the case, to furnish evidence on the matter of possible late sequelae for both scientific and medico-legal purposes. Follow-up observation is important. — Reprinted from *Industrial Hygiene* (April, 1943), a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

*Bagley, C., Jr. Blood in cerebrospinal fluid: resultant functional and organic alterations in central nervous system; experimental data. *Arch. Surg.* 17:18 38, 1928.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

ADAMS—CHANCEY ADAMS, MD, of Concord, died May 11. He was in his eighty third year.

Dr Adams received his degree from Bowdoin Medical School in 1891, and for several years served on the staff of the United States Marine Hospital, Staten Island, N. Y. He was a member of the New Hampshire Medical Society, the American Medical Association and of the Surgical Staff of the Margaret Pillsbury Hospital.

MISCELLANY

NOTES

Dr Frank H. Lahey, of Boston, chairman of the Directing Board of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians, was recently awarded an honorary degree (D.Sc.) by Boston University.

Dr Granville A. Bennett, associate professor of pathology at Harvard Medical School, has accepted the appointment of professor of pathology and bacteriology at Tulane University of Louisiana School of Medicine. He has already left Boston to assume his new position.

BOOK REVIEWS

Essentials of Pathology. By Lawrence W. Smith, MD, and Edwin S. Gault, MD. With a foreword by James I. King, MD. Second edition. 4°, cloth 960 pp. with 695 illustrations and 13 color plates. New York: D. Appleton-Century Company, Incorporated 1942. \$10.00.

The authors depart from the usual textbook style in presenting pathology to students by employing the case method. It seems to the reviewer that, although it is valuable for a second year student to know something about the clinical aspects of cases that have furnished pathologic specimens, to devote nearly half the written text to case histories is carrying it too far, especially when the clinical summary often has no relation to the pathologic lesion. For example, hyaline degeneration of the splenic arterioles is illustrated by describing the case of a fifty-nine year-old colored woman who died of a cerebrovascular accident; this includes a history of influenza in 1918, a physical examination of the heart, the details of the paralysis, the autopsy findings of rheumatic heart disease with terminal bacterial endocarditis, and other observations irrelevant to splenic arteriolar hyalinization. The clinical summaries and general autopsy findings are so lengthy and often so noncontributory that the important item may be overlooked or more attention paid to the non-related observations, especially by a second year student. Although this point is admitted by the authors in their preface by the statement, "Unless our histories and physical examinations are complete in every instance we as physicians may overlook some much more serious condition than that for which the patient consults us," the reviewer believes that routine completeness in clinical histories and physical examinations belong in the field of clinical medicine and not in that of pathology, and that it is much more important for the second year student to spend his time learning the fundamentals of pathology than to hurry him into clinical medicine, since he will spend the rest of his life in the clinic but may never again have an opportunity in pathology.

In selecting cases to illustrate pathologic lesions, the authors not infrequently use unusual or rare examples. For instance, actinomycosis is illustrated by involvement of the fallopian tube, bronchiectasis by an upper lobe lesion in an autopsy specimen, when one in a surgically removed lower lobe would certainly have been a better choice in these days, hyperparathyroidism by a rare case of diffuse *wasserhelle* primary parathyroid hyperplasia, instead of the more usual adenoma, and chondroma by the incidental finding of several cartilaginous nodules in the lung, when a bone lesion would have been more appropriate.

The book is a valuable adjunct to the student examining microscopic slides in the laboratory, because it contains at the end of each case history a detailed microscopic description of the lesion in question with a photograph of the section. Unfortunately the latter are often several pages away from the microscopic descriptions. The one danger of this method of teaching, however, is that the student may not explore the slide sufficiently himself before referring to the text.

The book contains many more photographs than the usual textbook of pathology and might almost be called an atlas rather than a textbook. The great majority of these are photographs of sections, of which many are excellent, most are fair and some are very poor. There is a paucity of gross photographs, and what there are were usually taken from fixed specimens, which are not too convincing. Practically all the roentgenograms have been poorly reproduced.

The text, itself as its name indicates, is merely the essentials of pathology, and for that reason alone the book cannot be recommended as the only one necessary for a second year student. It will prove useful to have as a sort of laboratory manual in addition to the ordinary text book.

Neurology. By Roy R. Grinker, MD. With the assistance of Norman A. Levy, MD. With a chapter on brain tumors by Paul C. Bucy, MD. Third edition. 4°, cloth, 1136 pp., with 416 illustrations. Springfield, Illinois: Charles C. Thomas, 1943. \$6.50.

The five years that have passed since the second edition of this book have brought many changes to neurology. The author has rewritten many of the sections of his standard textbook and thoroughly revised others. The whole book has been reprinted on an entirely new format and in general is considerably improved. Unfortunately the size has been increased to over 1100 pages. In spite of this the publisher has reduced the price from \$8.50 to \$6.50, an unprecedented procedure, largely possible because of the wide sale of this popular book. It means a considerable saving to medical students, the chief users of this book, and also it allows a book on a specialty to be published at a rate sufficiently low to make it attractive to the general practitioner in internist and surgeon.

The book is extremely sound particularly in the history of physiology and neuropathology, fundamentals which are essential to an understanding of the nervous system and its diseases. This edition can be highly recommended and the author and publisher are to be congratulated on their forward steps respectively, in revising the text and in reducing the price of this publication.

Some minor errors that were found in previous editions have been corrected, and the bibliographies in general have been brought up to date. It has been impossible for the author to follow all the advances in neurology during the five-year period. This results in a deficiency in some of the sections, particularly those covering the clinical aspects of neurology. This is not a matter of criticism, for no single author can possibly follow all the advances in a rapidly moving specialty. If defects are found it must be put down to inability of any one person to keep up with a vast and rapidly accumulating literature.

War Medicine: A symposium. Editor, Winfield S. Pugh, M.D., commander (M.C.), U.S.N., retired; associate editor, Edward Podolsky, M.D.; technical editor, Dagobert D. Runes, Ph.D. 8°, cloth, 565 pp., with 100 illustrations, 13 tables, 10 diagrams and 8 charts. New York: Philosophical Library, Incorporated, 1942. \$7.50.

A republication of articles published in the current medical literature forms the basis of this book. They cover a wide range of papers on surgery, aviation and naval medicine and general medicine. The contents have been chosen with care and represent some of the best of the war literature. The book is well printed and should prove to be a useful volume for physicians both in and out of service. It appears to be somewhat hastily put together and lacks an index. The exact place and time of the individual contributions are not given. The lack of sound editing is partly compensated for by excellent reproduction of the illustrations.

Extramural Teaching of Preventive Medicine and Public Health. By Alfred Korach, M.D. *Medical Bulletin of the University of Cincinnati* (Vol. IX: October, 1942). 4°, cloth, 144 pp., with 4 tables. Cincinnati, Ohio: University of Cincinnati College of Medicine, 1942. \$1.50.

This is an account of outside instruction for medical students at the University of Cincinnati. It was organized under the Department of Preventive Medicine, and apparently takes complete advantage of the opportunities available in Cincinnati and its environs. Reference to industrial medicine, toxicology and industrial health is omitted. Furthermore, there is no mention of correlation with other parts of the curriculum, as there certainly should be in an enterprise which includes handicapped people (orthopedic surgery), the blind (ophthalmology), prenatal obstetric care (obstetrics), child nutrition (pediatrics) and public-health nursing and social services (medicine). All of these, if possible, should be correlated in the student's mind. These things are not pointed out as defects, but as opportunities for further development of what is obviously an admirable effort, which is carefully and completely presented in this volume.

Mental Illness: A guide for the family. By Edith M. Stern, with the collaboration of Samuel W. Hamilton, M.D. 8°, cloth, 134 pp. New York: The Commonwealth Fund, 1942. \$1.00.

This little book is clearly written and of great usefulness to the families of patients with mental disease. It gives a lucid account of the nature of mental illness, with

practical advice regarding such matters as hospitalization and the technic of getting a patient admitted to a hospital. This information is of real value to the families of those who are mentally sick, in that the legal procedure in mental cases is mysterious to them, although, in reality, simple. There is also a good account of the various types of treatment, including shock, prolonged sedation, psychotherapy and occupational therapy, all of which is simply presented and yet adequate for the layman. The prospects for recovery and the care of the patient at home are also discussed; and generally speaking, the advice is sound, sensible and kindly.

An excellent glossary at the end of the book deals with such terms as organic mental disorder, orientation, parole and remission — all of which are mysterious until explained and, when understood, help the family to follow adequately the physician's comments and advice.

The author is to be congratulated on a useful, common-sense book, free from dogmatism and bias.

NOTICES

REMOVAL

DR. ATTILIO C. PERONA announces the removal of his office from 12 Linden Street, Norwood, to 529 Washington Street, Dorchester.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The annual meeting of the American Board of Obstetrics and Gynecology was held at Pittsburgh, Pennsylvania, from May 20 to May 25, at which time 108 candidates were certified.

A number of changes in regulations and requirements were put into effect. Several of these are designed to broaden the requirements for candidates in military service. Examples are the allowance of a stipulated amount of credit toward special training requirements for such men who are assigned to general surgical positions and special training allowances on a preceptorship basis for men assigned to obstetric or gynecologic duties in military hospitals and working under the supervision of diplomates or recognized obstetrician-gynecologist, as well as credit toward the time-in-practice requirement of the board for time in military service.

The board no longer requires a general rotating internship, but now accepts a one-year intern service, although the rotating internship is preferable. Such services must be in institutions approved by the Council on Medical Education and Hospitals of the American Medical Association. Lists of such institutions are published regularly in the Educational Number of the *Journal of the American Medical Association*.

The privilege of reopening applications by candidates who have been declared ineligible has been extended to two years from date of filing the application, instead of one year.

The board has ruled temporarily to excuse men in military service from submission of case records at the stipulated examination times, thereby permitting them to proceed without further delay with their examinations.

(Notices continued on page xiv)

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HOW BEST TO EAT UNDER WAR CONDITIONS*

FREDRICK J. STARE, M.D.[†]

BOSTON

NUTRITIONAL requirements in wartime do not differ from those of peacetime, except in so far as some persons may be more active in wartime and hence have somewhat increased requirements. Furthermore, the nutritional requirements for Bostonians do not differ from those for Londoners or other people, although they may be satisfied by entirely different foods. These statements seem simple and obvious, but many forget them under the emotional strain of war. It is of more national importance in time of war that nutritional requirements be obtained, than it is in peace because good nutrition is an essential factor for maintaining and improving the health of civilian and armed forces and their morale. With proper leadership, intelligent planning and common sense on the part of administrative officials and the public, there is no reason—barring unforeseen crop failure—why the people of our country and our armed forces cannot be well fed from a nutritive viewpoint, and why we cannot at the same time contribute measurably to the feeding of people in other countries. Undoubtedly our choice of foods will be restricted, as well as the quantities of them, but this need not interfere with nutritional well-being; in fact, the individual nutritional status of many persons may actually improve by intelligent application of well-established nutritional facts.

Essentially the question of how best to eat under war conditions involves a consideration of two problems. What are the nutritional requirements for health, and how may we obtain these from available foods? As part of the second problem, there should be some understanding of the effect of processing on the nutritional quality of the food.

Before considering the nutritional requirements for health, I shall mention briefly what food does

for us and why we need it. We need food for body building and repair, we need it for body heat and energy, and we need it for supplying ready made, or enabling us to make, substances such as vitamins, enzymes and hormones for regulating body processes, including growth and reproduction, and for the normal functioning of organs, nerves and muscles. In addition to these food functions that are necessary for health, the eating of good food is one of the pleasures of life. Not many will deny the taste appeal, the satisfaction, the sheer enjoyment derived from eating an excellent dinner. Do not forget the pleasure value of food when some publicity seeker proclaims that soon our daily nourishment may come from a few small capsules or pills.

The nutritional requirements for good health, whether in war or peace, consist of adequate amounts of protein, fat, carbohydrate, certain minerals, certain vitamins and water.

It may be well at this time to emphasize a point that is frequently overlooked by many nutritionists, namely, that there are no absolute requirements known for any of these food factors. All the requirements spoken of are relative ones. The amount of protein needed depends on the amount of fat and carbohydrate in the diet; the amount of fat needed depends on the amount of carbohydrate and protein in the diet, the amount of calcium needed depends on the amount of other basic minerals in the diet; and the amount of thiamine needed depends on the amount of carbohydrate and fat in the diet. Hence, tables of nutritional requirements usually refer to an average person on an average diet. The figures given are optimal, as they should be for optimum health—sufficiently high to allow a generous margin of safety for individual differences in requirements, and to cover any errors in the present-day knowledge of nutrition. Thus, if the adult requirement for protein is given as 70 gm per day, this should not be

*A synopsis of one of a series of free public lectures given by the Faculty of Medicine of Harvard University at the Peter Bent Brigham Hospital.

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understood to imply that if one gets 50 gm. a day he will be malnourished. That depends on the rest of the diet and on one's personal physical status. If the adult requirement for vitamin A is given at 5000 units per day, this does not imply that if one receives 3000 units per day he will be malnourished. This amount may or may not be sufficient, but in any case he is skating on thinner ice. There is less margin of safety so far as the vitamin A requirements are concerned, and unless the person concerned gets enjoyment merely from being contrary, or has good evidence that 5000 units of vitamin A is too high a value for the average adult, better health would probably be enjoyed by receiving the amount suggested by a majority of the best nutritionists of today.

Protein is the principal nitrogenous constituent of animal and vegetable tissue. It is the basic constituent of protoplasm. Protein may also, in the body, be converted into carbohydrate and be used as a source of energy. Chemically, the proteins are large, complex molecules. In the process of digestion these large molecules are broken down into units that are simpler from a chemical viewpoint, and ultimately into what are called amino acids. There are approximately twenty-four known amino acids, and of these about half are termed essential. This means that the body tissues cannot make them and that they must be obtained ready-made from food. The biologic or nutritional value of proteins is considered in terms of their content of essential amino acids. Thus, casein, the principal protein of milk, is a complete protein; it is of high biologic value because it contains all the amino acids known to be essential to life. Zein, the protein of corn, is an incomplete protein; it is of lower biologic value because it lacks two of the essential amino acids. Generally speaking, proteins of animal origin, which include not only meat but milk, eggs, fowl and fish, are of higher biologic value than are vegetable proteins. But vegetable protein is perfectly adequate in so far as it supplies many of the essential amino acids, and it supplies other amino acids (as does animal protein) that, although not essential for life, certainly contribute to body economy. In peacetime most people obtain the main part of their protein from animal meat, particularly the so-called "muscle meats" of steers, pigs and sheep, and a smaller amount from meats such as liver, heart, kidney, tongue, fish and poultry, from milk and cheese or from vegetable protein. The answer to the question how and where protein requirements should be obtained in wartime, when muscle meats may be scarce or unobtainable, is obvious. Vegetarians are certainly not upset

about meat rationing, and George Bernard Shaw is an excellent example of long-lasting, vigorous health. They obtain protein not only from vegetables but from milk, cheese, eggs and fish. For the average adult, 1 gm. per kilogram of body weight—which for the average adult means 70 gm.—is a sufficient amount. It should be noted that this 70 gm. is of protein, not of meat. Only about 25 per cent of meat is protein, the other 75 per cent being water.

Fats are the most potent source of energy. When completely utilized they furnish twice the energy value per unit amount that carbohydrates or proteins do. A most important function is that they serve as carriers for the fat-soluble vitamins, which from the viewpoint of the practical nutrition of normal adults means only vitamin A. Experimentally, certain unsaturated fatty acids have been found to be essential for the rat. It is not known whether man needs these unsaturated fatty acids and whether he must obtain them from food, but it is most unlikely that these acids are important in practical adult human nutrition.

When it is said that vitamin A is the only fat-soluble vitamin of importance in practical human nutrition, this does not mean that the other vitamins are not needed, but only that they are not of importance in planning normal adult diets. This may be for a reason such as a small requirement that is easily obtained from almost any foods, or the synthesis of certain nutrients, such as vitamin K, by intestinal bacteria.

Fat is obtained in the human diet from both animal and vegetable sources. Butter and lard are the principal animal fats consumed; the vegetable oils most commonly used are those derived from corn, soybeans, olives, peanuts and coconuts. Hydrogenated cottonseed oil is the basis of such products as Crisco. Margarines, such as oleomargarine, are made from animal or vegetable fats. When vitamin A is added to the margarine, it is fully as nutritious for adults as is butter.

How much fat is needed in the diet? This too depends on one's physical status and on what else is eaten. Generally the fat in the diet is more than the protein and less than the carbohydrate, ranging in amount from 100 to 150 gm. But one can get along reasonably well with less fat provided that sufficient carbohydrate is available to meet energy needs and that a source of the fat-soluble vitamin A is also available. This is conveniently possible, since the body can make vitamin A from carotene, the yellow pigment present in many green and yellow vegetables.

Carbohydrate is plentiful in the diet, in fact too much so for many people. Its main sources are

flour, sugar, rice and starchy vegetables, particularly potatoes. Fruits also contain variable amounts of sugar.

How much carbohydrate is needed in the diet? One really needs none so far as nutrition is concerned—there is nothing "essential" about carbohydrate, but it is the cheapest source of energy available. Also large amounts of it can be stored in the body in the form of glycogen, and also as fat, since the body can form fat from carbohydrate. Because of the ease with which carbohydrate may be obtained, and its low cost, large amounts are used in the diet. A sedentary person consumes 200 to 250 gm. per day, whereas a person doing hard physical labor may consume three to five times that amount.

Certain inorganic or mineral elements are just as necessary to health as are protein, certain vitamins or water. Twelve minerals are known to be necessary in good nutrition; these are calcium, iron, phosphorus, copper, sodium, potassium, magnesium, manganese, iodine, chlorine, sulfur and zinc. Many of these are necessary only in minute amounts. Sodium and chlorine are needed in relatively large amounts, but are easily supplied by the use of table salt. In the inorganic elements the diet is most likely to be deficient in calcium and iron, and among those who live in the inland areas between the Alleghenies and the Rockies, an iodine lack is possible. In such locations the use of iodized salt in cooking and for the table is recommended. Iron is obtained from meat, particularly liver. It is also contained in eggs, leafy green vegetables, potatoes, dried fruits and whole grain cereals. Milk and cheese are the only really good food sources of calcium, although small amounts are drawn from most vegetables and from meats. The diet will certainly be low in calcium unless enough milk in some form is present.

It is sufficient to say that mineral requirements are well met through the use of iodized table salt, ample portions of the foods listed as good sources of iron and some form of milk for calcium.

Of the fat soluble vitamins, A, D, E and K, only vitamin A is of practical importance in the nutrition of the normal adult. The best sources of vitamin A are liver, egg yolk, whole milk, cream and butter, but many persons do not eat liver frequently, or do not drink much milk or eat many eggs, and with butter difficult to obtain where will one get vitamin A? Fortunately dark-green leafy vegetables and yellow vegetables contain a substance called carotene, which in the body is converted into vitamin A. Another safety factor is the capacity of storing large amounts of vitamin A, particularly in the liver and kidneys. Thus, if in the summertime green leafy and yellow vegeta-

bles and summer butter are consumed in large amounts, sufficient vitamin A is stored to help one through the winter.

Of the water soluble vitamins, ascorbic acid and several of those of the vitamin B complex are required. It is important to know that one does not have the ability to store the water-soluble vitamins for any length of time, as is the case with the fat-soluble vitamins. Thus they must be provided for regularly in the diet.

Ascorbic acid is obtained chiefly from citrus fruits—oranges, grapefruit, lemons and tangerines—and from tomatoes or raw cabbages. Small but significant amounts are derived from potatoes if they are cooked in the jacket. This is necessary because ascorbic acid is easily destroyed by contact with the air, particularly at an elevated temperature. From the practical viewpoint a diet will be deficient in vitamin C if citrus fruits, tomatoes or raw cabbages are not included in it. Half a grapefruit or half a glass of orange juice—that is, about 4 ounces—will furnish approximately two thirds of the daily requirement; about twice as much tomato juice is required. Pineapple juice is a poor source of vitamin C.

The various members of the vitamin B complex are obtained chiefly from meats, which include fowl and fish, particularly liver and kidney, from milk and cheese, from legumes, such as peas, beans and peanuts, and from whole grain cereal or bread. The members that are known to be necessary in human nutrition and that must be considered in the selection of food are thiamine, riboflavin and niacin. There is little doubt that other members are required in human nutrition, but their importance in food planning is yet to be determined. From the viewpoint of practical nutrition, the sources of thiamine, riboflavin and niacin are also the sources of the other members of the vitamin B complex. Milk and liver are the best sources of riboflavin, and without either the diet may be low in this substance.

Water need only be mentioned. It serves as a solvent and is vitally concerned with all phases of health. Actually, as is well known, one can live longer without food than without water.

I shall now discuss somewhat more practically how one can obtain an adequate protein supply from a variety of food. This is important for a number of reasons; protein is vital for health, whereas, strictly speaking, fat and carbohydrate are not; further restrictions are apt to involve the protein foods; and the protein foods are good carriers of many of the minerals and vitamins.

At present the weekly adult meat ration approximates 1½ pounds, or 540 gm. The amount of bone varies with different cuts, but assuming an

average proportion of 20 per cent, this gives 672 gm. of meat per week. As already stated, only about one fourth of meat is actually protein, the other three fourths being mostly water. Thus, the ration yields 168 gm. of protein per week, or about 24 gm. per day. This amount is obtained from about 100 gm. of meat, and for comparison it might be mentioned that one average-sized pork chop has approximately this weight. It is therefore seen that with the present meat ration one should be able to obtain about one third the desired amount of protein. What additions can be made from available foods so as to raise the protein intake to at least 70 gm.?

Table 1 shows that it is a fairly simple matter to obtain the desired 70 gm. of protein per day, or to exceed this level. It should be emphasized that fish, sea food and poultry are approximately equal to the rationed meats in nutritive value. It is also important to note the richness in protein of beans, particularly the soybean. In addition, cheese, peas, lentils, peanut butter and the

Butter, or olcomargarine enriched with vitamin A, in the amounts ordinarily used does not contribute more than about one tenth of the daily requirement of vitamin A. In an average diet, dark-green leafy and yellow vegetables supply about half the vitamin A requirement, and butter, milk, eggs and tomatoes furnish the other half. Dried apricots are an excellent source of vitamin A, but they are now unobtainable, since the armed forces take most of the supply. It should be emphasized that lettuce is not a dark-green leafy vegetable. In the amounts usually consumed, it contributes small amounts of minerals and of certain vitamins, but its nutritional quality is highly overrated. Green-leaf lettuce obtainable in the spring and summer is far superior in nutritional quality to the bleached lettuce of wintertime, but it is inferior to such dark-green leafy vegetables as broccoli, spinach, turnip greens, kale, beet greens, Swiss chard, collards, dandelion greens, endive, escarole, mustard greens and watercress. Green peppers are also a good source of carotene — that is, of provitamin A.

TABLE 1. Means of Obtaining the Desired Daily Amount of Protein (70 gm.) and a List of Foods Containing Appreciable Amounts of Protein.

SOURCE OF DAILY PROTEIN REQUIREMENTS		FOODS RICH IN PROTEIN	
FOOD	PROTEIN gm.		
Rationed (or unrationed) meat	24	Rationed meat (30 gm. per serving)	
Milk (1 glassful)	8	Unrationed meat — fish, sea food and poultry (30 gm. per serving)	
Egg (1)	7	Beans (6 to 11 gm. per serving)	
Bread (4 slices)	10	Lentils (9 gm. per serving)	
Vegetables (2 servings)	8	Cheese (6 to 10 gm. per serving)	
Legumes (1 serving)	7	Peas (6 gm. per serving)	
Potato (1)	2	Peanut butter (5 gm. per table-spoonful)	
Miscellaneous foods (fruit, salad, dessert, cereal etc.)	4	Cooked whole-grain cereals (4.5 gm. per serving)	
Total	70	Ice cream (4 gm. per serving)	
		Bread (2.5 gm. per slice)	

cooked cereals are good sources of protein. It should be clear how a diet adequate in protein can readily be planned from available foods. In fact, if unrationed meats were added to the rationed list and the daily allowance cut in half, one could still have a diet nutritionally adequate in protein provided there was a plentiful supply of the vegetable proteins and of milk.

As has been mentioned, it is important to stress the protein foods, because they are vital to health and because they generally serve as a good supply of minerals and of the vitamin B complex. They do not, however, assure an adequate supply of ascorbic acid or of vitamin A. Ascorbic acid will be adequately supplied in ordinary diets only when some citrus fruit or juice, tomatoes or tomato juice, or raw cabbage is consumed daily. For vitamin A one must depend to a considerable extent on dark-green leafy and yellow vegetables.

Although the nutritional quality of food depends to a considerable extent on the type of soil on which the food is grown, and on weather conditions, it is principally influenced by the following factors: the length of time from harvesting the food until it is processed; the length of time and the temperature of any blanching treatment or any process in which the food is in contact with water; contact with bright sunlight or unusual exposure to air, as would be obtained if the food were chopped or finely divided; the reaction of the food — that is, whether it is slightly acid or alkaline; and the degree and duration of heat used in processing the food.

Minimum values for the above, consistent with adequate preparation of the food, and an acid reaction are desired to preserve the maximum nutritional quality. The nutrients that are most likely to be lost in processing are ascorbic acid, thiamine, riboflavin and vitamin A. Accordingly, in home cooking, excesses of heat and of water should be avoided, and water that is added in cooking should be used over again for soups or gravies. Baking soda should not be added to the cooking water, and there should be a minimum amount of stirring. The pressure-cooker or steam type of cooking utensil is best from the viewpoint of maintaining nutritional quality.

Most commercially canned food is of a high nutritional quality, approaching that of the freshly harvested product, and is frequently superior to that of raw food obtained at many markets and that of home-canned food. The reason for this is that the food is harvested primarily for canning, is brought directly to the factory and is completely

processed within three or four hours, whereas the food that goes to market may not be bought until the next day or next week. Commercially canned food usually receives a short blanching with boiling water or steam, and is then cooked in a sealed container, which minimizes contact with the air. The cooking is usually at a high temperature and for a relatively short period. It should be emphasized that the brine or liquor of canned vegetables contains a considerable portion of the water soluble nutrients. It should not be discarded, but should be used as a sauce with the vegetable or in the preparation of gravies.

Frozen food likewise has a high nutritional quality. Here, too, the food is harvested primarily for freezing, and is processed a short time after picking. It is important to know that in the freezing process the cells are usually ruptured, and that when the food is warmed there is a rapid loss of oxidizable and water-soluble nutrients. Hence it is advisable that frozen food be cooked and consumed promptly after being thawed.

One reads much these days about dehydrated food, and there is no doubt that a good sized dehydrating industry has developed to meet the wartime demand for dehydrated food, which obviously offers an enormous saving in transportation. But the dehydration of food on a commercial scale is a new and growing industry. There are numerous techniques for dehydrating food, and changes are constantly being made to improve the process. Thus, to discuss accurately the nutritional quality of dehydrated food will be impossible until the technical process of dehydrating has been sufficiently stabilized so that analyses for nutritional quality today will apply to foods purchased next month. Important problems other than the actual dehydration of food are vitally concerned with dehydrated food; some of these are loss of nutrients during storage, protection from insects, packaging, rehydration and palatability of the end product. There has actually been insufficient experimental work on the nutritional quality of dehydrated foods to warrant any authoritative statement applicable to dehydrated food in general. Years of research by manufacturers of canned food have brought about improvements in food processing to the point where the nutritional value of commercially canned food is often equal to that of the fresh product from which it is made. There is every reason to believe that similar research efforts applied to dehydration will produce equally good results.

It might be appropriate to mention that the nutritive quality of food served in many restaurants is distinctly inferior to that of home cooked food because it is frequently prepared several

hours in advance and is kept warm, or is warmed over. This involves considerable contact with heat and air—hence, the inferior nutritional quality of the food. Losses in vitamin C are high, and losses in thiamine and riboflavin are probably considerable.

Much has been heard in the last few years about the superior nutritional quality of whole-wheat and enriched flour as compared with plain white flour. In the process of milling wheat to prepare flour the outer husk and the germ of the wheat kernel are removed. This results in considerable loss of nutrient value, specifically of the vitamin B complex, of minerals, particularly iron, and of some protein. Whole wheat flour and, generally speaking, other dark flours retain more of these nutrients than does white flour, which results from a thorough milling. Because white flour and breads made from it are of poor nutritional value, and because a large portion of the American public prefers white bread, attempts were made to improve the flour. These procedures have been of two kinds: first, the addition of synthetic preparations of certain members of the vitamin B complex and of iron, and second, technical improvements in milling procedures so as to prepare a light colored flour but one that still retains more of the nutrients than is done in the usual milling process. Bread made from enriched flour is termed "enriched bread." It is definitely superior in nutritional quality to white breads made from unenriched flour, but still does not measure up to whole-wheat bread.

It is of interest that Order No. 1 signed by the Secretary of Agriculture in his capacity as Food Administrator included a statement that beginning January 18, 1943, all white bread must be enriched to approved nutritive standards. This is a most important and desirable order, and will do much to improve the nutritional quality of the diet of many people. It is to be hoped that improvement in milling procedures will be vigorously pursued so that flours of light color and good keeping quality and yet of superior nutritional standards will be available.

Table 2 gives a basic outline for a daily diet of high nutritional value. A great variety of diets may be had within the framework of this outline, and from available foods. If one cannot get rationed meat, unrationed meat may be used; if one does not like milk, or cannot get it, cheese, if available, should be substituted, or vegetables of high protein value particularly beans, lentils and peas.

The frequent statement that all that is necessary to have good nutrition is to eat natural foods

go far enough. It should be supplemented by adding, "a *proper combination* of natural foods." And one must know what combination of foods will provide a nutritionally sound diet. More emphasis is frequently placed on the use of natural foods than on their proper combination. Different natural foods differ greatly in their nutrient content, and it is easy to have a diet of natural foods and yet have an inadequate diet. For example,

TABLE 2. *Outline of Daily Diet for an Adult.*

Food	QUANTITY REQUIRED
Milk	.2 glassfuls or 1 glassful and 1 serving of cheese
Meat	1 or 2 servings — rationed or unrationed (fish, fowl or sea food)
Eggs	3 or 4 per week
Vegetables	
Potato	1 or 2 servings
Dark green leafy or yellow	1 or 2 servings
Legumes	1 or 2 servings
Fruits	..2 servings, 1 being citrus (or tomato)
Cereals	..4 slices of whole grain or enriched bread, or less bread and a serving of whole grain or enriched cereal
Fats and sweets	To meet energy requirements, after the above foods have been consumed
Iodized salt	To season food

beets contain a small amount of thiamine and pork a hundred times more, yet they are both natural foods. Milk contains a small amount of niacin and peanuts two hundred times more, yet both are natural foods. It should be evident that a proper combination of foods is necessary for good practical nutrition, and in wartime, when certain foods are restricted, one should know what combination of available foods will provide a diet of high nutritive quality.

In conclusion, it may be appropriate to answer a few questions concerning butter and milk that many people are asking. Is oleomargarine of equal nutritive value to that of butter? For practical human nutrition oleomargarine enriched with vitamin A is fully equal to butter in nutritional quality. There are many eminent nutritionists who would not make such a statement, but I know of no experimental evidence applicable to human nutrition that contradicts it. In fact, oleomargarine with a standardized amount of vitamin A added to it may be superior to winter butter

in vitamin A value because the vitamin A content of butter varies with the content of this vitamin in milk, and winter milk usually has a lower level than does summer milk.

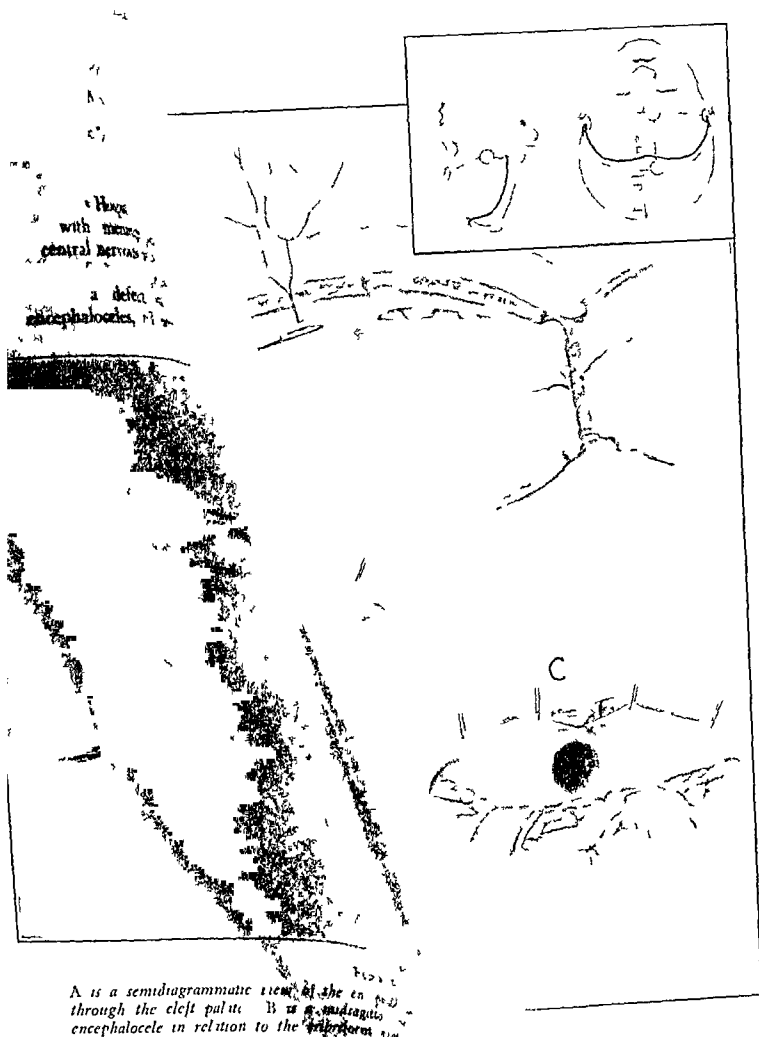
Another question often asked is, Must an adult drink a pint of milk each day to have good nutrition? It is not necessary for anyone to drink milk, but the plentiful addition of milk to any diet is one of the best ways to improve its nutritional quality. Many people think of milk merely in terms of supplying calcium. This is wrong. Milk supplies a good amount of protein, which is of the highest nutritive value. It is also the best-known source of riboflavin; in fact, without milk in the diet, either as a beverage or ice cream or in cooked food, it is most difficult to obtain the desired amount of riboflavin. Furthermore, milk is a fair source of thiamine, and whole milk contains considerable vitamin A. Hence, in addition to being the best food source of calcium it is an excellent source of many other necessary nutrients, particularly some of those in which the usual American diet is low. Persons who do not drink milk or eat good amounts of cheese would definitely improve their diet by consuming a pint of milk per day.

A question that might be asked is, If milk is rationed, what then? Milk, whatever amount is available, should go first to infants, pregnant and nursing women, children and adolescents, and then to other adults.

* * *

In summary, nutritional requirements in wartime do not differ from those of peacetime, but it is of national importance in time of war that a determined effort be made to see that all our people and our allies are well nourished. Good nutrition is an important factor in maintaining and improving the health of the civilian and armed forces and their morale. Secondly, to have good nutrition, it is necessary to understand to some extent the nutritional requirements desired for good health, and particularly, from the practical viewpoint, to understand what combinations of available food each day are necessary to supply these requirements, and how to prepare this food with minimum loss of the nutrients it contains.

25 Shattuck Street



A is a semidiagrammatic view of the encephalocele in relation to the foramen magnum. B is a frontal view of the encephalocele. C is a cross-section of the skull base showing the foramen magnum.

the dotted lines the
has been opened

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nose. The case reported here is the only one
which interior herniation of the brain
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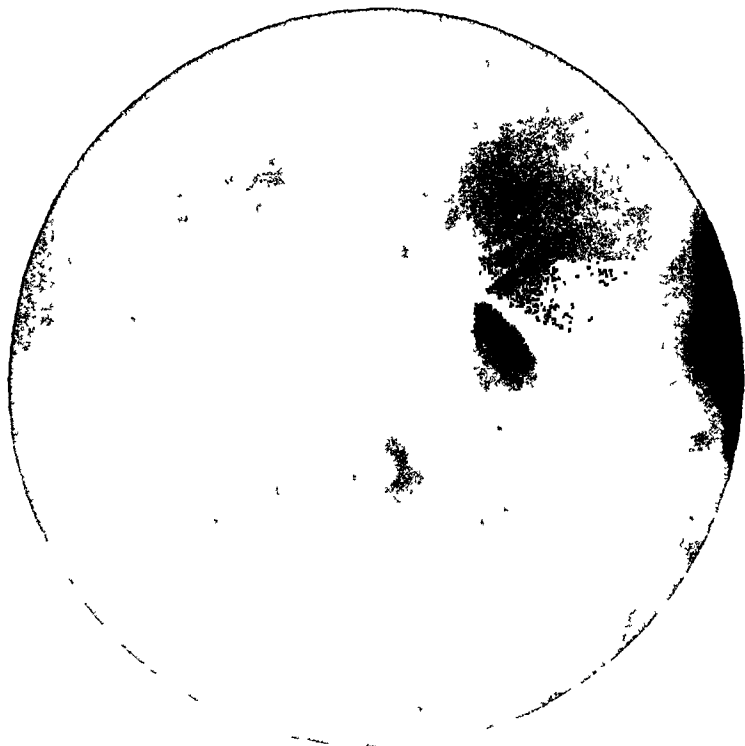


FIGURE 2.

Sinus roentgenogram showing the absence of bony structures of the cribriform plate and of the ethmoid cells on the left.



FIGURE 3.

Lateral pneumoencephalogram showing a normal ventricular system and subarachnoid spaces.

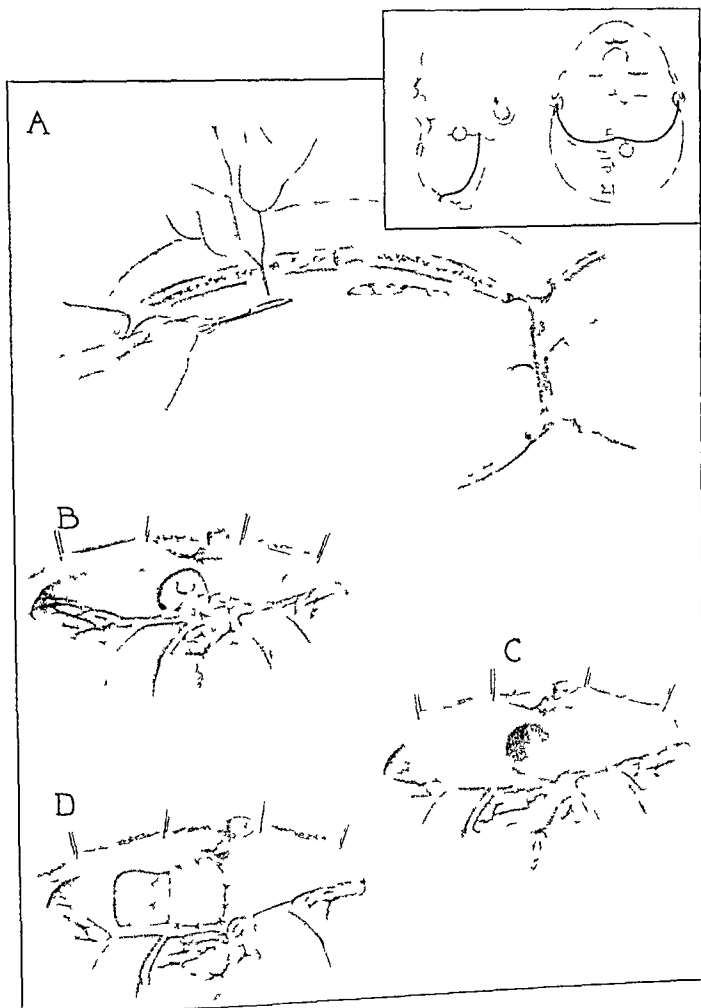


FIGURE 4

In the insert the solid line indicates the site of incision and the dotted lines the limits of the right and left frontal bone flaps. In A the dura has been opened on either side of the longitudinal sinus at the anterior limit of the exposure. In B, the pedicle of the herniated brain at its origin from the left frontal pole has been exposed after division of the longitudinal sinus and filx and retraction of the frontal lobes. C shows the inside of the meningocele sac after amputation and removal of the herniated brain. In D the dural flap has been reflected from the floor of the frontal fossa across the defect in the cribriform plate and has been sutured to the crista galli.

visible in the nasopharynx. Partial removal had been done at three months of age, with no untoward sequelae. Intranasal removal with a tonsil snare was carried out and recovery was uneventful, but drainage from the nostril persisted.

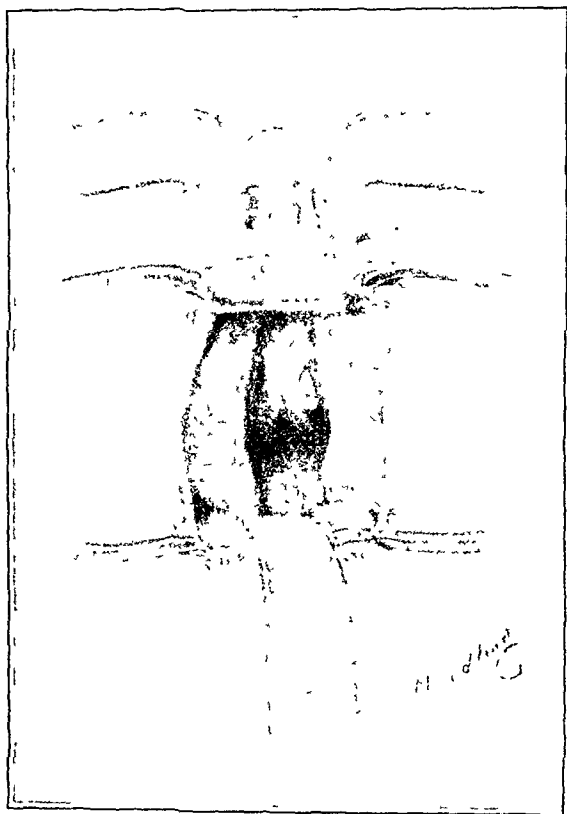


FIGURE 5.

This shows the shrinkage of the meningocele sac in the nasopharynx, with resultant improvement of airway, as seen on the seventh postoperative day.

One year after operation the patient developed severe meningitis, which responded to chemotherapy, but he showed a slight recurrence in the upper anterior nares and continued to have rhinorrhea. McGillicuddy suggests that an intracranial approach to the pedicle was probably indicated.

The clinical problems of diagnosis and especially of neurosurgical management of this rare anomaly seem to make a report of the following case desirable.

R. A. N. (C. H. 242961) was first seen on June 7, 1940, at the age of 23 days. He was referred to the Children's Hospital because of a right incomplete harelip, cleft palate and a redundant skin tab over the tip of the coccyx. No family history of congenital anomalies could be elicited. He was delivered normally at full term and there were no postnatal disturbances. Examination revealed the above findings, and was otherwise negative except for a midline dimple in the skin of the sacral region. Plastic repair of the harelip was carried out uneventfully and the patient was discharged home.

He re-entered the hospital for repair of the cleft palate on September 28, 1942, the operation having been twice postponed in the interval because of mild upper-respiratory infection associated with nasal discharge. The interval history was otherwise negative and the patient's development appeared to be normal. Physical examination revealed a healthy child whose head was of normal size and shape; the fontanelles were closed. The nose showed flattening of the right external nares. The left nostril was almost completely blocked by a smooth, bluish-gray, fluctuant, soft-tissue mass medial to the inferior turbinate and extending posteriorly. A probe could be passed around the mass on all sides, so that it seemed to be attached superiorly. The mass did not shrink after the topical application of adrenalin.

There was a well-healed scar of the harelip repair with a good cosmetic result. A wide cleft of the palate extended from the uvula to within 1 cm. of the alveolar ridge anteriorly. A moderate growth of adenoid tissue was visible on the posterior pharyngeal wall. On either side of the nasal septum, smooth, bluish-gray, fluctuant masses were seen protruding over the margins of the cleft palate, that on the left measuring 1 by 1.5 cm. and that on the right 0.5 by 1.0 cm. (Fig. 1). These masses were observed to vary somewhat in size at different examinations.

Laboratory studies revealed normal urine and blood. A blood Hinton test and an intracutaneous tuberculin (1:1000 dilution) test were negative. Spinal-fluid studies were within normal limits.

Roentgenograms of the skull and sinuses showed absence of the normal bone structures in the region of the cribriform plate, with obliteration of most of the ethmoid cells (Fig. 2). A pneumoencephalogram showed the ventricular system to be quite normal in size, with no evidence of an unusual collection of air near the cribriform plate and no shift or defect in the lateral or third ventricles (Fig. 3).

On October 9, 1942, under Avertin and ether anesthesia, exploration of the frontal fossa was carried out through a right frontal bone flap exposed by a coronal incision. Extradural and intradural exploration over the right frontal lobe visualized a projection of dura-covered brain through a defect in the cribriform plate, and the diagnosis of anterior encephalocele was thus confirmed. However, this exposure was obviously inadequate for surgical removal of the lesion, so that routine closure was carried out.

The postoperative course was uneventful and on the 6th postoperative day, again under Avertin and ether anesthesia, the coronal incision was reopened. The right frontal bone flap was again elevated on a lateral hinge of periosteum. Two more burr holes were placed in the left frontotemporal region and a left frontal bone flap extending across the midline was elevated on a left periosteal hinge (Fig. 4).

The dura was then opened on either side of the sagittal sinus as far anteriorly as possible (Fig. 4A) and the sinus was ligated and divided. As the falx was divided down to the crista galli, an unusual number of large tributary veins leading into the anterior end of the sagittal sinus were divided between silver clips. Both frontal poles were retracted posteriorly, and it became easy to visualize a herniation of brain extending from the left frontal lobe downward and forward through a defect in the cribriform plate, which displaced a rudimentary crista galli toward the right (Fig. 4B). The herniated brain could not be delivered from its extracranial compartment,

so that it was amputated from the frontal pole and subsequently removed piecemeal from the meningeal sac (Fig. 4C). This sac, which could then be invaginated into the frontal fossa, was, however, left intact in the position in which it was found in order to avoid communication of the meninges with the nasal cavity. The inner surface of the meningocele sac was superficially

masses lateral to the olfactory sacs. The lateral masses ossify first into the spongy bone of the ethmoidal labyrinths. Fibers of each olfactory nerve pass between the unjoined mesial mass and the adjacent lateral mass. Later, cartilaginous trabeculae surround these bundles of nerve fibers

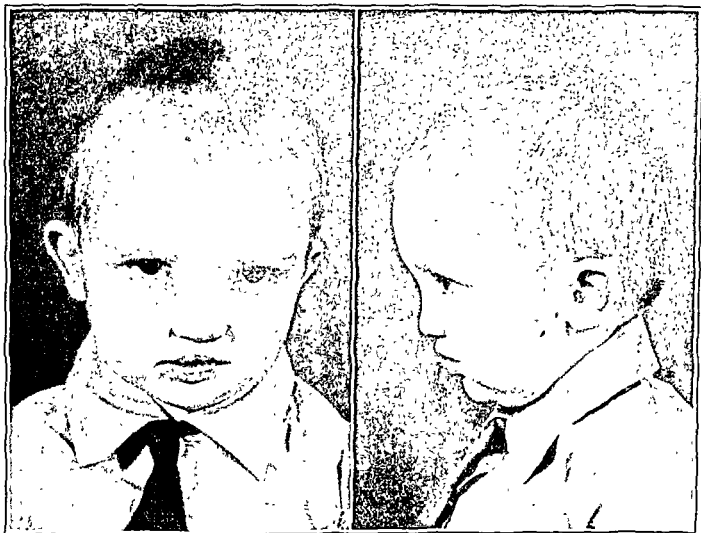


FIGURE 6.

These photographs of the patient were taken two months postoperatively.

coagulated with endothermy current in the hope of speeding its obliteration.

A flap of dura and periosteum was next raised from the floor of the frontal fossa laterally, turned on a hinge, and sutured across the defect to the crista galli (Fig. 4D). Routine closure of the dura, bone flaps and scalp was carried out.

The postoperative course was again uneventful. On the 7th postoperative day, examination under Avertin anesthesia revealed the masses in the nasopharynx to have shriveled markedly (Fig. 5). The mass in the left nostril was smaller but not necrotic. The nasopharyngeal airway was much improved. On the 14th postoperative day, the patient was discharged to the Wellesley Convalescent Home for 4 weeks, at the end of which time repair of the cleft palate was planned.

In this case, several associated developmental defects in the facial area were present. A cleft palate resulted from failure of the lateral palatine processes to unite properly. Failure of the right maxillary process to fuse with the median nasal process resulted in a right incomplete harelip. According to Arey,⁶ the embryonic ethmoidal cartilage consists of a mesial mass and of paired

and interconnect the three masses. When these perforated parts of the completed ethmoid become ossified, they are designated the cribriform plates. Presumably, failure of these cartilaginous trabeculae to form or to ossify resulted, in this case, in a defect in the cribriform plate that permitted herniation of the brain into the nose and nasopharynx.

This case proved interesting not only because of the rarity of the lesion but because the even more uncommon association of the cleft palate provided an excellent view of what might otherwise have been a hidden anomaly. The possibility and danger of mistaking such a lesion for a polyp or tumor of extracranial origin and of attacking it surgically through the nose or mouth are self-evident. The development of a spinal-fluid leak into a contaminated field followed by meningitis would be an almost certain complication.

The case is also interesting because the patient was an otherwise apparently normal boy (Fig. 6) with a series of congenital anomalies, all suitable

for satisfactory surgical therapy. The importance of delaying the repair of the cleft palate until an adequate airway had been established by removal of the encephalocele should be emphasized.

The surgical approach outlined and illustrated in this report proved highly satisfactory, and is recommended for attacking lesions of this kind in the region of the cribriform plate.

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HEMORRHAGE AND PURPURA CAUSED BY DICOUMARIN*

Report of a Case

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FIRST isolated and then synthesized by Link and his associates,¹ dicoumarin is the active principle in spoiled sweet-clover hay causing hemorrhagic disease in cattle. A threefold purpose motivated its introduction as a possible useful therapeutic agent: the prevention of thrombosis, especially postoperatively, the alleviation of thrombosis that had already been established² and the treatment of peripheral vascular diseases.³

The patient described herein received prolonged treatment with dicoumarin and developed severe and alarming but transient hemorrhagic and purpuric symptoms. Since this patient was observed, another case has been reported in which similar symptoms appeared after prolonged treatment with dicoumarin from this same batch.⁴

CASE REPORT

A 50-year-old housewife weighing 137 pounds was admitted to the Knickerbocker Hospital on September 28, 1942, complaining of weakness and progressively increasing painless hematuria of 1 month's duration. There was no history of any other bleeding, purpura or jaundice. The previous history included a hysterectomy, repair of cystocele and rectocele and hemorrhoidectomy at another hospital on August 19, 1942, following which the patient lost 6 pounds. There was nothing else of importance in the family, social or previous medical history. Two days after admission purpuric patches appeared on both upper extremities and bleeding from the gums started.

Physical examination at that time revealed an anxious-appearing and pallid woman. The pulse was 112 and thready, and the rectal temperature was 100°F. Blood oozed from the gingival margins of the gums and dripped from the upper teeth. The patient expectorated numerous pea-sized blood clots. There was no epistaxis.

The purpuric manifestations, which appeared only on the upper extremities, were bilateral and occurred as bluish raised areas covering the entire dorsum and proximal phalanges of both hands, round patches 2.5 cm. in diameter over each styloid process and blue-black sub-

cutaneous areas 5 cm. in diameter over the flexor and extensor surfaces of both elbows. There were no petechiae and no telangiectases. The heart was normal. The blood pressure was 125/90. The lungs were clear throughout. Neither the liver nor the spleen was palpable. Moderate tenderness was elicited over the region of the urinary bladder. There was no lymphadenopathy. The urine was frankly bloody with innumerable red cells per low-power field. A blood Wassermann reaction was negative.

Venous blood examined shortly after collection in Wintrobe's oxalate mixture revealed the following counts: red cells 2,620,000; hemoglobin (Sahli) 50 per cent (7.25 gm.); white cells 8300, with 4 per cent nonsegmented neutrophils, 64 per cent segmented neutrophils and 32 per cent lymphocytes. Platelets numbered 370,000 per cubic millimeter. The clotting time (Lee and White) was 16 minutes, and clot retraction appeared normal within a few hours. The bleeding time (Duke) was 13 minutes. A capillary-fragility test (blood-pressure cuff maintained midway between the systolic and the diastolic pressure for 5 minutes) yielded negative results, nor did slapping or pinching the flexor surface of the forearm produce petechiae. During the time the venous-blood return was impeded by this test, the distal purpuric areas increased in size. The prothrombin percentage obtained by comparing the prothrombin time (Quick) of a normal control with that of the patient was 19. The hematocrit was 26 cc. of cells per 100 cc. of blood. The blood plasma was not icteric.

Smears made from marrow aspirated from the sternum by the puncture method showed the following percentages of cells: myeloblasts, 0.1, myelocytes, 21.9, young forms, 28.0, nonsegmented neutrophils, 11.0, segmented neutrophils, 1.7, eosinophils, 4.6, lymphocytes, 15.0, plasma cells, 1.2, normoblasts, 16.5 (basophilic cells, 0.2, polychromatophilic cells, 11.6, orthochromic cells, 4.7).

The correlation of the clinical findings and the blood picture at this time was difficult. The bone marrow changes were nonspecific. There was no platelet reduction, no capillary fragility and no abnormality in clot retraction. However, the bleeding time was prolonged, the coagulation time was increased, and a marked prothrombin deficiency was evident, associated with purpura and bleeding from the gums.

Although the patient's blood was Group A, cross-matching with two available Group A donors and one Group O donor was unsuccessful because of the appear-

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ance of macroscopic agglutination. Particularly, a few drops of the patient's blood spread over a glass slide dried (rather than clotted) into large macroscopic clumps.

The patient was promptly transfused with 250 cc of citrated banked blood plasma without any untoward reaction. Twelve hours following this transfusion bleeding from the gums ceased and no new purpuric patches appeared.

Further investigation of the history revealed that the patient had received dicoumarin in almost daily doses

purpuric manifestations ceased when the prothrombin percentage reached 20. It is possible that 20 per cent represents a critical level below which phenomena appear. The findings suggest, however, the involvement of another factor, since the prothrombin percentage was only 24 when the bleeding time had fallen to one minute and the purpuric and hemorrhagic activity had been

TABLE 1 Summary of Data

TIME	RBD CELL COUNT X 10 ⁶	HEMO- GLOBIN CONTENT %	WETTL CELL COUNT X 10 ³	PLATE- LET COUNT X 10 ³	BLED- G TIME min	COAGU- LATIN- G TIME min	COT- RETICU- LATION	CAPILLARY FRACTURE TYPE	TRAIL C P LAR SENSITIVITY	PRO- THROMBIN LEVEL %	CLINICAL DATA
Before dicoumarin	4.0	85	8.9								
After dicoumarin											
1st day	3.6	64	10.0								Hematuria, purpura
2nd day	2.6	50	8.3	3.0	13	16	Normal	Normal	Increased		Hematuria, increased purpura, bleeding from gums, plasma transfusion (250 cc)
3rd day	—							No mal	Increased	19	Hematuria, purpura, no bleeding from gums
4th day	1.1	30	14.0	1.0	20	10	No mal	No mal	Increased ()	20	Hematuria, purpura, blood transfusion on (500 cc Group O) fever to 103.4°F
5th day	1.6	30	9.0	9.0	8	10	Normal	No mal	No mal		Hematuria (slight), purpura, blood transfusion on (500 cc Group O) fever to 104.8°F
7th day	2.4	42	6.2	22.0	1	10	No mal	No mal	Normal	24	No hematuria, purpura
9th day	2.1	42	22.8	23.6	2	8	Normal	No mal	Normal	61	Purpura (slight), jaundice (mild), blood transfusion on (500 cc Group A) fever to 106°F
11th day	2.3	45	1.4							80	No purpura, no jaundice
19th day	3.0	60	9.0							—	Discharge

of 100 mg. During the 32 days immediately prior to hospitalization a total of 2800 mg had been administered. Exhibition of dicoumarin was instituted 2 weeks postoperatively subsequent to the occurrence of fever and chills which had been ascribed to embolization. Hematuria which appeared after repeated catheterization was first noted on the day dicoumarin was started but prior to its administration and persisted with increasing severity until 8 days after its withdrawal.

Two subsequent transfusions with 500 cc of banked blood, Group O were complicated by moderately severe febrile reactions (Table 1). A third transfusion with fresh Group A blood was followed by chills, fever and collapse after 100 cc had been injected. This last reaction inaugurated a 3 day episode of borderline jaundice without the appearance of bile hemoglobin or excess of urobilin in the urine. Regrouping and cross matching established the compatibility of this transfusion. Reactions to other transfusions in the hospital at this time were nil.

The return of the blood findings to more normal levels and the patient's slow convalescence are indicated in detail in Table 1.

DISCUSSION

The clinical findings and blood picture resulting from dicoumarin toxicity have been ascribed to the development of a severe hypoprothrombinemia.¹ In this case bleeding from the gums and

quiescent for four days. It is difficult to assume that the change in the prothrombin percentage from 20 to 24 was alone responsible for the drop in bleeding time from 20 minutes to 1 minute and the cessation of all symptoms. Possibly the phenomenon described below may be of assistance in elucidating the mechanism of the purpura and hemorrhage.

It is noteworthy that the lobe of the ear, the site chosen for the Duke test for bleeding time, became blue and swollen. This phenomenon is known to occur in thrombocytopenic purpura. But, unexpectedly, the increased capillary fragility and diminution of platelets usually associated with thrombocytopenic purpura were not present.

With the same procedure as that employed in the Duke bleeding time test the forearm was punctured to a depth of 1 cm by a 26-gauge needle. The site chosen was an area free from visible blood vessels 7 cm below the bend of the elbow. Within a few minutes the area surrounding the needle puncture wound became black and blue. After the initial bleeding had ceased, a tourniquet was applied proximally and the purpuric area perceptibly increased in size. At the

same time the other purpuric areas distal to the tourniquet became larger.

On removing the tourniquet, a 2 cm.-wide encircling band of purpura was found. Its origin was obviously traumatic and resulted from the application of the tourniquet. The blood vessels must therefore have been pathologically sensitive to trauma, since it is not usual for the application of a tourniquet to produce purpura. This pathologic sensitivity of the blood vessels to trauma is probably distinct from capillary fragility.

It is possible that the purpuric areas appearing over the bony prominences of the hands, wrists and elbows and the hemorrhage from the gums were traumatic in origin and were indeed manifestations of this underlying sensitivity of the blood vessels to trauma. The positive needle-puncture tourniquet test described herein probably represents an abnormal sensitivity of the vascular bed to trauma. This test is not influenced by the presence of adequate numbers of platelets or of an increased capillary fragility. Whether the hypoprothrombinemia alone or another principle in the dicoumarin is the cause of this vascular sensitivity to trauma is not known.

The needle-puncture tourniquet test for traumatic vascular sensitivity was tried on several patients, with interesting results. In a case of hypertension with pyelitis, there was a negative traumatic vascular-fragility test as judged by the nonappearance of a purpuric areola, but a positive capillary-fragility test with the appearance of many petechiae. The bleeding time in this patient was $1\frac{1}{2}$ minutes. A patient with terminal subleukemic

myelosis and many purpuric patches over the abdomen had a positive needle-puncture tourniquet test but the capillary-fragility test was negative. The bleeding time was 2 minutes. A third patient developed a small hematoma from the puncture of an underlying blood vessel. The needle-puncture tourniquet test was negative on the other arm. In none of the other cases was either of these tests positive. No control developed areolas around the needle-puncture wound, despite the proximal application of a blood-pressure cuff at a level midway between the systolic and the diastolic pressure for five minutes.

SUMMARY

A patient is described who received 2800 mg. of dicoumarin in thirty-two days and developed hemorrhagic and purpuric manifestations with a prolonged bleeding time and a marked prothrombin deficiency without platelet reduction, capillary fragility or abnormality in clot retraction.

It is suggested that dicoumarin toxicity induces not only a hypoprothrombinemia but also an increased sensitivity of the vascular bed to trauma.

A needle-puncture tourniquet test to elicit sensitivity of the vascular bed to trauma is described.

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MEDICAL PROGRESS

EPIDEMIOLOGIC ASPECTS OF FOOD BORNE DISEASE (Concluded)

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BOSTON

FOOD POISONING

Botulism

BOTULISM is due to the production of a heat-labile toxin formed by the germinating spores of *Clostridium botulinum* in underprocessed canned foods. Two varieties, Types A and B, are usually encountered in the United States; recently, cases due to Type E were reported in California. To quote Dack²:

War conditions in 1917-18 served as a stimulus to preserve more food, and at that time the danger of botulism was not recognized. Hence, considerable spoilage from underprocessing was encountered, with an occasional outbreak of botulism. Research to determine the cause of spoilage showed that the cold pack method of processing foods for home canning, as recommended by the government at that time, was entirely inadequate to prevent botulism.

During the ten years from 1931 to 1940, inclusive, there have been an average of 11 outbreaks each year. From 1899 to 1941, according to Meyer,¹⁴⁹ there were 359 outbreaks, of which 4 were in Massachusetts, 1 in Connecticut, 1 in Maine and the remainder outside the New England states. Geiger, Dickson and Meyer¹⁵⁰ found that up to 1922, 62 per cent of the outbreaks in California were due to home canned apricots, pears, string beans, asparagus and corn and commercially packed ripe olives and spinach. Only 24 per cent were due to animal products, which are the usual source of botulism in Europe. Dack² analyzed the foods responsible for 359 outbreaks between 1899 and 1941. The foods most frequently involved were string beans (80 outbreaks; 3 with commercial canning), corn (36; 1 with commercial canning), spinach or chard (21; 10 with commercial canning), beets (16; 2 with commercial canning), asparagus (13; none with commercial canning), olives (13; 12 with commercial canning), beans (10; none with commercial canning). The amount of acidity in the food is an important factor in determining the limits of

growth of *Cl. botulinum*. Growth is uncertain at pH 5.4 or lower. The food may or may not give evidence of spoilage, such as a foul odor or a sharp taste.

Hunter, Weiss and Olson¹⁵¹ observe that prior to 1935 botulism was unknown in South Dakota and *Cl. botulinum* could not be isolated from the soil. In that year, however, the disease made its appearance as an epidemic of limber neck among chickens fed on home canned corn that showed signs of spoilage. The following year, a family outbreak occurred. String beans that had been home-canned by the cold pack method were slightly foamy and faintly rancid. They were rinsed in cold water and served to 5 persons. Four ate them and died within forty-two hours; 1 did not and kept well. Many chickens ranging in the back yard died of limber neck, presumably after drinking from a puddle into which the kitchen sink drained. Type A *Cl. botulinum* was isolated from the beans. These authors conclude that canning by the cold pack method should be discontinued if further outbreaks of botulism are to be avoided.

Twenty cases in Tennessee prior to 1939 are reviewed by Tucker and Swanson,¹⁵² who report 2 cases caused by eating home canned okra and possibly home canned beans. Type B *Cl. botulinum* was isolated from the okra, and Type B toxin was found to be present in both the beans and the okra.

In Oregon, Watson¹⁵³ treated 16 cases of botulism, with a case fatality rate of 30 per cent. He states that large doses of bivalent (Types A and B) antitoxin are imperative in the treatment of the disease. Prompt intravenous administration, followed by repeated intramuscular injections, was described as the most satisfactory procedure. Oxygen administration is recommended by this author, who used the respirator when respiratory paralysis seemed imminent. Most writers, however, consider the specific treatment of the disease unsatisfactory. The mortality rate is usually 60 to 70 per cent.

Geiger¹⁵⁴ reports a family outbreak of botulism in California involving 3 cases, with 1 death. The family of 6 ate for supper macaroni prepared

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with commercially canned mushroom sauce designated as "Italian style," milk, apples and oranges. The sauce was not heated but was poured directly over the cooked macaroni before serving. The three children who were affected obtained the first servings. Three other members of the family ate the same meal, but did not become sick. The incubation periods in the 3 sick children were ten, seventeen and 20 hours respectively. The can was not a "swell" (a can bulged by fermentation) and the sauce was normal in appearance and taste. It had been manufactured in California from mushrooms that had been dried in Yugoslavia and shipped in sealed cans. In manufacture, the cans (No. 1 size) had been heated at 245°F. for forty-five minutes. The pH of other cans varied from 4.2 to 4.9. Type E *Cl. botulinum* was obtained from the sides of the empty tin.

The New York State Department of Public Health¹⁵⁵ calls to the attention of health officers the possibility of an increase in cases of botulism from home-canned foods, because of the larger numbers of Victory gardens and the subsequent home canning of foods. Between 1922 and 1941, there were 36 cases, with 14 deaths in upstate New York. The department urges consumers of home-canned foods to boil them for at least fifteen minutes after removal from the containers. Data collected from the health departments of the New England states revealed that botulism¹⁵⁶ is rare in this region. From 1920 to 1942, there were no known cases or deaths due to botulism in any of the states except Connecticut, which reported 5 cases—2 in 1922, and 1 each in 1925, 1933 and 1942.

The United States Department of Agriculture bulletin entitled "Home Canning of Fruits, Vegetables and Meats"¹⁵⁷ contains detailed instructions not only for the correct handling and processing of foods, but also for their safeguarding against spoilage from *Cl. botulinum* and other dangerous bacteria.

Botulism can be prevented if home canning is properly performed. Special care must be taken in the immediate future because underprocessing of home-canned products may occur frequently now that home canning is stimulated by the rationing of commercially canned foods. Proper precautions must be taken by all canners, especially by those who are canning for the first time. The fruits and vegetables should be fresh and firm, and should be thoroughly washed, cleaned and canned as soon as possible after harvesting. Non-acid food such as vegetables, meat, poultry and fish should be processed in a pressure cooker, according to Faust,¹⁵⁸ of the United States Depart-

ment of Agriculture. If a cold-pack method is employed in home canning, the food should be re-boiled for ten to fifteen minutes before tasting or eating. Canned food that is foul in odor, has an off or sharp taste, or gives off gas on being opened should be discarded, preferably without tasting, since the toxin is extremely powerful and may cause severe illness even in minute doses.

Staphylococcal Poisoning

Dack² states: "Staphylococcus food poisoning, like botulism, is produced by a toxin formed in the food before ingestion. It is probably the most common of all food poisonings, although we have no knowledge of the number of cases occurring annually, since it is not reportable." The enterotoxin is heat-stable, even after boiling for thirty minutes, and chlorine in palatable amounts is not effective in destroying it.

The literature on staphylococcal food poisoning is profuse. The laboratory procedures and the characteristics of the enterotoxin are described by numerous authors.¹⁵⁹⁻¹⁶⁵ Dack¹⁶⁶ describes some of the laboratory procedures that can be used to determine whether the strain of *Staph. aureus* concerned is one that can produce enterotoxin. Not all staphylococci give rise to food poisoning; however, if *Staph. aureus* is found in abundance in a suspected food, this is presumptive evidence that it is the offending agent. Final proof of whether the isolated strain is a food-poisoning type rests on animal experimentation.

It is often found desirable to classify a strain of *Staphylococcus* in order to obtain positive evidence in an outbreak. If specimens that are isolated from the food, from the food handler and from the vomitus of patients are identical, this is the best proof of the sequence of the outbreak. Durfee¹⁶⁷ classified 110 strains and describes methods that are employed in this procedure, such as agglutinative and polysaccharide-forming qualities.

Favorite and Hammon¹⁶⁸ studied the production of staphylococcal enterotoxin and alpha hemolysin in a special medium, a procedure that is useful in determining the toxicity of strains isolated from food-borne outbreaks. Hammon¹⁶⁹ describes a practical intravenous cat test for the evaluation of staphylococcal enterotoxin. This method is adaptable for use in large public-health laboratories.

Although numerous outbreaks due to the organism have been described, only a few will be cited. Geiger and Crowley¹⁷⁰ report an outbreak due to commercially prepared egg-and-olive sandwiches contaminated by a carrier. Chason and Waite¹⁷¹ studied one due to buttermilk. Dorling¹⁷² tells how an elderly woman infected a can of soup

from a whitlow of the left thumb. The soup was left standing at room temperature for seven days, then heated and eaten. Three hours later the woman became ill, with vomiting and diarrhea, and died on the same day. A strongly hemolytic, coagulose-positive strain of *Staph aureus* was isolated from the empty can and from the stomach and intestinal contents. In Worcester, Massachusetts,¹⁷³ a woman prepared soup from a dehydrated mix and left it standing for twenty eight hours, it was then heated and eaten by the woman and her granddaughter. Both were ill with severe nausea, vomiting and diarrhea three hours later. *Staph. aureus* was isolated from the left over soup. Two other packages of the same lot of dehydrated soup were free of staphylococci.

Coughlin and Johnson¹⁷⁴ reviewed 17 staphylococcal outbreaks, with 1227 cases, between 1935 and 1939 in upstate New York. All were traced to cream filled pastry. Five of the outbreaks, responsible for 60 per cent of the cases, were from a single bakery. Chocolate éclairs and cream puffs were most commonly involved, and contrary to popular belief, the outbreaks occurred in the colder months as well as during the summer. The authors recommend the rebaking of filled pastry and prompt sale as methods of control. The New York State Department of Health reported the following recent food poisonings due to staphylococci. Twenty-eight patrons of a first class restaurant in an upstate city became ill five hours after a meal, with profuse vomiting, diarrhea and marked prostration. The vehicle was hollandaise sauce, which is made from butter, egg yolks, lemon juice, water and salt. Sixteen persons in New York City were served a dinner at a hotel in March, 1942. From three to eight hours later, all but one became ill with diarrhea, cramps, nausea and vomiting, which lasted for two to three days.¹⁷⁵ The only person who was not ill had not eaten hollandaise sauce. The sauce had been prepared at 10 a.m. the day of the dinner and had been kept on the steam table until ready to use at 8 p.m. Two persons who ate the sauce at noon and a third who ate it between 5 and 6 p.m. were not made ill. The department urges scrupulous cleanliness in preparing and handling hollandaise sauce and other foods of this nature. Over 165 persons, principally nurses and employees of a large upstate general hospital, became ill with an explosive onset of gastrointestinal symptoms six hours after eating turkey salad.¹⁷⁷ The meat used had been left over from roast turkey served forty-eight hours previously. Laboratory examination demonstrated a hemolytic *Staph aureus* in large numbers, both in the salad and in the meat from which it was prepared. Twenty persons, employees

of an upstate industrial plant, became ill with nausea, vomiting and diarrhea after eating cream-meringue pie at the plant cafeteria.¹⁷⁸ The pies were approximately eighteen hours old when the first person was served. The manner in which the pies were infected was not determined.

In Worcester, Massachusetts, 180 persons in a large war industry became ill with nausea, vomiting, chills and prostration following a meal in the plant cafeteria.¹⁷⁹ The same strain of *Staph aureus* was isolated from the throat of a food handler, from the ham served the employees and from the vomitus of one of the patients. The ham had been kept at 90°F for four to six hours in thermos containers.

During July, 1941, 71 cases of staphylococcal poisoning occurred in nineteen families. Terzich¹⁸⁰ traced the source as improperly pasteurized milk sold by two retail milk dealers. Geiger¹⁸¹ reports an outbreak in California in which there were 110 reported cases in twenty eight families. The patients became ill after eating cream custard cakes from a single bakery. The sanitary facilities there were highly inadequate, giving ample opportunity for the ubiquitous staphylococcus to contaminate the custard.

Two interesting outbreaks are reported from Hamilton, Ontario, by Roberts, Deadman and Elliot.¹⁸² Twenty one persons in five families ate a custard filled pastry purchased from a bakery. All the employees of the bakery were carefully examined, and cultures were taken. *Staph. aureus* was isolated from 4 employees, from cream pie, lemon roll and vanilla slices and also from jam tarts, pastry bags, and milk from a can in the bakery. The same bakery was involved in another outbreak two months later, when there were 8 persons ill in four families. Wilson¹⁸³ studied the organisms isolated from this bakery. The staphylococcus persisted in the nose and throat of the employees of the bakery for three weeks, but was absent six weeks after the outbreak. In 1941, Hamilton had another outbreak of staphylococcal food poisoning. A butterscotch pie baked in the restaurant where it was served was incriminated. Staphylococci were obtained from the pie, the pastry big tip and the vomitus of a patient. From studies by Wilson,¹⁸⁴ these strains and one isolated from the baker were found to be identical. The same author¹⁸⁵ has described the symptomatology, differential diagnosis and treatment of staphylococcal food poisoning. The signs and symptoms vary only slightly in degree. Onset is rapid and occurs from one to five hours after ingestion of the contaminated food. The symptoms are dizziness, nausea, abdominal cramps and vomiting, lasting usually only a few hours but in

severe cases several days. The temperature is usually normal, the pulse is increased, and there are frequently cold sweats. Diarrhea may occur simultaneously with the vomiting or be delayed for several hours. Patients may become markedly dehydrated. (In an autopsy on a patient who died from acute staphylococcal food poisoning, the outstanding finding was an extensive and marked lack of body and tissue fluids; an adequate fluid intake might have saved the patient's life.) The acute symptoms generally last only a few hours, but in severe cases there is prostration and recovery may be delayed for several days. During this period a temperature of 100°F. is not unusual. In *Salmonella* infections, the onset is usually delayed for twelve hours or more, and fever is not an uncommon finding. These are the two most important characteristics whereby staphylococcal food poisoning can be differentiated from *Salmonella* infection. The treatment is symptomatic, and in severe cases is essentially that of shock and dehydration, which may become quite marked.

Slocum¹⁸⁶ discusses the differentiation of staphylococcal and *Salmonella* food poisoning. In the former the incubation period is short, usually two to four hours, and the onset is characterized by abdominal cramps or pain, nausea, vomiting and diarrhea. Fever is not a usual finding. The duration averages six to eight hours and recovery is rapid. In *Salmonella* infection, the incubation period is six to twenty-four hours and fever is common. The duration is much longer and recovery is delayed for days. Slocum states that *Salmonella* infection is commoner in Europe than staphylococcal food poisoning, whereas in the United States the reverse holds true.

Chemical Poisoning

Food-borne chemical poisoning is comparatively rare as contrasted with staphylococcal food poisoning. However, the clinical syndromes of these two types are closely similar. Both are characterized by a short incubation period. The onset of nausea, vomiting and diarrhea is sudden. Sweating, abdominal cramps and a normal or subnormal temperature are characteristic in both. In cadmium or fluoride poisoning, the incubation period is usually somewhat shorter. The only way, however, to distinguish between these two food poisonings is by analysis of the vomitus and the suspected foods. The chemicals most likely to be found in food are fluorine, cadmium, arsenic and chemical refrigerants, such as methyl chloride, escaping from defective mechanical refrigerators. Dack² lists the various chemical poisons and the characteristics of the gastrointestinal upsets that follow their ingestion.

In Massachusetts, an outbreak was traced to a discharged employee who added sodium fluoride insecticide to corn-meal batter in a grudge against his employer.¹⁸⁷ There were no fatalities. Lidbeck et al.¹⁸⁸ describe an acute sodium fluoride poisoning involving 263 cases and 47 deaths in a mental hospital in Oregon. Sodium fluoride was added to scrambled eggs by a patient who confused a barrel of sodium fluoride, an insecticide, with one of powdered milk. Many of the inmates did not eat the eggs because of the bad taste. The incubation period was short, the chief symptoms being nausea, vomiting and diarrhea, leading to collapse. Where patients were ill over a longer period of time, the pupils became dilated, the pulse was thready, respirations were shallow and unlabored, the heart tones were weak, and the skin was cold, moist and cyanotic. Other symptoms were paralysis of the muscles of deglutition, carpopedal spasm and spasms of the extremities.

In a New York reform school, 69 of 96 persons who ate chocolate pudding for dessert suddenly became ill with nausea, followed by repeated vomiting, severe cramplike pain in the epigastrium and later by one or two loose movements.¹⁸⁹ Weakness and sweating were prominent symptoms. Headache, salivation and lacrimation were present. The temperature was normal or subnormal. Investigation revealed that an inmate kitchen helper had added a handful of roach powder containing sodium fluoride to one hundred gallons of chocolate pudding. The amount of sodium fluoride varied in different samples of the pudding, ranging from 0.1 to 0.3 per cent. Since a serving consisted of 200 gm. of pudding, each patient ate 0.2 to 0.6 gm. of sodium fluoride, an amount that is below the lethal dose of 3 gm. Legislation has been passed in New York State requiring the coloring of all fluoride containers and insecticides by prescribed dyes. Similar requirements should exist in all states.

Recently, cadmium poisoning has become prevalent as a result of the replating of metal food utensils with alloys containing this metal. The United States Public Health Service¹⁹⁰ has prepared a special bulletin on this subject. In New York, according to Coughlin and Johnson,¹⁹¹ between 1938 and 1941 4 outbreaks of cadmium poisoning occurred, 3 of these from acid foods prepared in cadmium-plated food utensils, and 1 from ice cubes in a cadmium-plated tray in a leaky refrigerator where the escaping refrigerant dissolved some of the cadmium. As a result of these outbreaks, the use of cadmium in the replating of food utensils is no longer permitted in New York. Cangelosi¹⁹² describes 3 outbreaks, with 208 cases, in the Fleet Marine Force operating in the

Caribbean in 1941. The principal findings were abdominal pain, nausea, vomiting, normal or sub-normal temperature, sweating and headache. Recovery was rapid. All the patients drank coffee or lemonade made in cadmium-plated containers. Treatment consisted of the administration of warm water to encourage emesis, and, for those more severely ill, bismuth subnitrate and paregoric to control diarrhea. Measures were instituted to stop the use of cadmium in metal food containers. Frant and Kleeman¹⁹³ report 50 cases in 5 outbreaks, all due to drinking an acid liquid prepared in cadmium-plated containers.

Coughlin and Johnson¹⁹¹ cite the occurrence of several outbreaks of similar food poisoning in a number of hotels in the same area. Investigation revealed that these institutions were using the same brand of silver polish, which, analysis showed, contained sodium cyanide. This chemical can no longer be used in silver polish in New York.

Cox¹⁹⁴ points out that the use of insecticide or spray on fruits and vegetables carries a distinct danger because the chronic effects of continued ingestion of the lead, arsenic or fluorine in the liquid may result in illness. Prevention of this poisoning, he states, may be achieved by requiring that fruits be acid-washed or trimmed or otherwise conditioned so that they will reach the wholesale and retail markets with a legal tolerance of 0.05 gr. of lead, 0.025 gr. of arsenic and 0.02 gr. of fluorine per pound. The co-operation of growers, shippers and food inspectors is required in order to prevent chronic poisoning from insecticides and spray residues. Scott¹⁹⁵ discusses a case of arsenical hepatitis from spray residue on fruits and vegetables. Sampson¹⁹⁶ describes an outbreak of polyneuritis in South Africa due to the ingestion of triorthocresyl phosphate contained in cooking oil.

Shellfish Poisoning

Sommer and Meyer¹⁹⁷ describe a paralytic form of shellfish poisoning along the Pacific coast. The same type of disease has been reported from Nova Scotia, western Canada and Belgium. The poisoning is due to the presence of the dinoflagellate *Gonyaulax catenella*. The warm sun and the cold, nutrient waters along the Pacific Coast are responsible for an abundance of this organism in the summer. The poisoning is due to an alkaloid that is heat-stable in acid or neutral solutions but is gradually destroyed by boiling in alkaline solutions. One millionth of a gram is lethal for a mouse, and a few milligrams for man. The alkaloid is stored in the digestive glands of mussels and excreted over a period of weeks. The poison is not stored in the muscular tissue of the mussel. Ocean mussels and large varieties of clams on the

West Coast, including the Washington and pismo types, have been incriminated. Since 1927, there have been 346 cases and 24 deaths from mussel and clam poisoning along the Pacific Coast from Alaska to Mexico; all the cases occurred between May 15 and October 15. In July, 1936, there was a mussel-poisoning outbreak in Nova Scotia with 2 deaths. The symptoms begin immediately after the mussels are eaten. A prickly feeling in the extremities and tongue is followed by numbness. An ataxic gait and muscular inco-ordination progress to ascending paralysis and death from respiratory paralysis in two to twelve hours. Gastrointestinal symptoms are rare, except in severe cases, where there may be vomiting. There is no known antidote. Suspected shellfish should be packed in alcohol and sent to a laboratory for analysis.

METHODS OF CONTROL

The control of food-borne disease should be the concern not only of epidemiologists and other public-health officials, but also of all physicians, food handlers and citizens who wish to bring the war to a rapid and victorious end. Gastrointestinal diseases are a major cause of absenteeism in industry. McGee and Creger¹⁹⁸ determined that 18.6 per cent of 40,942 days of work lost by employees of a powder-company plant in New Jersey in 1941 were due to gastrointestinal disturbances. Of 5402 absences from work, 24 per cent were due to this group of diseases. Of the 7605 days lost from diseases of the digestive tract, 30.6 per cent were from gastrointestinal upsets and colon dysfunction and 4.1 per cent from enteritis and dysentery. Most of the absenteeism occurred early in the week—especially after week ends—and after holidays.

Food poisoning frequently disrupts large war plants. Moreover, the importance of dysentery among the military personnel cannot be overemphasized. The health officer, the industrial physician, the industrial manager, the food handler and the consumer himself play important roles in controlling food-borne disease. Underwood¹⁹⁹ states that one of the roles of public-health activity in the national emergency is to ensure "ordinary sanitation, safe water and milk supplies, protection of food supply, a sanitary method of excreta disposal and drainage." Boudreau,²⁰⁰ speaking of epidemic hazards in war, emphasizes that they are dependent on the nature of the war and the diseases prevalent in the area, such as typhoid fever and the dysenteries in Russia and the Balkans.

Health officers²⁰¹ are expecting an increase in food-borne disease acquired in public eating places as a result of the war. More people are eating in restaurants because of the rationing of food

and the placing of women in industry. Increasing difficulties are being encountered in restaurants; the lack of responsible personnel trained in the sanitary and proper handling of food, the overburdening of kitchen facilities, the unavailability of proper equipment and in some cases short cuts and improper methods in food processing are the principal causes of the increase in food-borne disease.

Municipal health departments are the chief agents responsible for the sanitation of food establishments. As Korff²⁰² explains, the primary objective of food-establishment inspection is the prevention of food poisoning and infections transmitted by foods. This entails the co-operation of the entire food industry. Training of commercial food handlers is an accepted method of developing safe and sanitary procedures in restaurants and other food-handling establishments. Many municipalities have developed such courses. In Texas²⁰³ the state has assumed this responsibility by means of itinerant instructors, and is convinced that the training is effective in improving the sanitation of establishments.

The perennial question of routine examination of food handlers always appears. In New York City, the finding of each typhoid-fever carrier by routine stool cultures of food handlers cost the city \$50,000; therefore, the examination of food handlers was discontinued in 1934.²⁰⁴ Fort Worth undertook routine examinations of food handlers, and expended \$353.77 for finding each typhoid-fever carrier.²⁰⁵ The local medical society finally concluded that it did not favor routine medical examinations of food handlers—the same conclusion that was reached in San Francisco. Most health authorities have now given up the idea of routine examinations of food handlers as impractical, and as involving an unjustifiable expense of funds that could be utilized for more effective methods of food control.

An important person in the control of food-borne disease is the consumer. The buyer must be aware of what sanitary and insanitary food handling means in relation to health.²⁰⁶ The health authorities must arouse in consumers a desire to trade in shops where food is handled in a clean and sanitary manner. Public opinion is a powerful influence on the commercial food handler; the storekeeper will sell the buyer whatever he demands. When the public is taught to demand safe, clean and sanitary food, properly processed and handled, food-borne disease will be reduced to a minimum.

The elimination of unhealthy animals is one of the veterinary's contributions to the control

of these diseases. McKim²⁰⁷ lists forty-six causes for which meat may be rejected or condemned as unfit for human consumption. The public-health engineer or inspector can do much to track down the mode whereby food may have become infected during processing, and take necessary measures to prevent a repetition.²⁰⁸ Fuchs,²⁰⁹ senior sanitary engineer of the United States Public Health Service, outlines the needs of adequate restaurant sanitation and discusses the provisions of a recommended ordinance regulating food and drink establishments.²¹⁰ This ordinance, or regulations based on it, has been legally adopted in seventy-four counties and by one hundred and twenty-three municipalities in nineteen states. These regulations provide minimum standards for the operation of a licensed or graded food-handling establishment. Inspection of all restaurants is required at least once every six months. If violations of regulations are not corrected after notice in a reasonable time, temporary suspension of the license or degrading (publicly displayed) and, if necessary, hearings, court action and fines are the methods of enforcement.

Horwood and Pesare²¹¹ made sanitary surveys of public eating places in Rhode Island and concluded that ignorance of accepted sanitary requirements and procedures as manifested by the managers and employees of public eating and drinking establishments is the most important single cause of insanitary practices in such places. The development of accepted sanitary procedures has been a concern of the Engineering Section Committee of the American Public Health Association, which publishes periodical reports on sanitary procedures, including standards for disinfection of dishes and utensils, evaluation of dishwashing machines, detergents and other aspects of food sanitation.²¹²

Regulations applying to food-handling establishments must, as Tiedeman²¹³ points out, be reasonable and practical, and must be enforced simultaneously with the education of the food handlers. In the hand-washing of dishes, temperatures of 120°F. for the wash water and 170°F. for the rinse water, thermostatically maintained, are considered adequate. Enough detergent must be used to remove properly all types of materials, in a short time. Soap, alkali, phosphates, silicates and sulfated alcohols are some of the detergents evaluated by Gilcreas and O'Brien.²¹⁴ Alkyl-dimethyl-benzyl ammonium chloride is recommended by Krog and Marshall²¹⁵ as an efficient sanitizing agent for the cleaning of eating and drinking utensils.

The Food and Nutrition Section of the Amer-

ican Public Health Association²¹⁶ surveyed ten public eating establishments to study the effect of an educational program and to evaluate methods. Mechanical washing of drinking glasses and eating utensils is better than hand washing because standards are more easily set, the temperatures of the wash water and the rinse water are higher, and the procedure is more easily controlled. If proper procedures in the hand-washing of dishes are used and clean towels are available, the number of bacteria per utensil can be reduced.

One of the most effective methods of reducing food-borne disease is the enforcement of proper personal-hygiene practices by all food handlers. Strict enforcement of hand washing before handling food, and especially after visiting the toilet, will do much to reduce typhoid fever, *Salmonella* and *Shigella* infections. These diseases are usually spread from the food handler's fingers that have been soiled by his excreta. Keeping the hands away from the mouth and nose and covering the mouth while coughing or sneezing, followed by washing the hands, covering foods when ever possible, refrigerating those that are perishable, reducing the interval between cooking and eating, eliminating food handlers with purulent wounds, boils or infections of the hands, preventing food handlers with sore throats from preparing food—all these will reduce most of the chances of contamination.

Since custard-filled and cream-filled pastries are one of the commonest vehicles for the transmission of food-borne disease, much research has been carried on in an endeavor to make these favorite items of the American diet safe for the consumer. One of the methods for controlling the ubiquitous staphylococcus in such pastries is rebaking, as described by Stritar, Jungewaelter and Dack.²¹⁷ Fifteen bakeries in Baltimore are described by Korff²¹⁸ as using this procedure and finding it satisfactory. Gilcreas and Coleman²¹⁹ state that rebaking for fifteen minutes at 216 to 220°C. (420 to 428°F.) destroys staphylococci and has no effect on the palatability or appearance of the pastry. These authors recommend that larger pastries be rebaked for twenty minutes. There seems to be no doubt that rebaking pastry will effectively eliminate a large proportion of food-borne disease, for which pastry has always been a common vehicle. Staphylococci and *Salmonella* organisms, the two bacteria most frequently found, will thereby be destroyed.

Cathcart, Ryberg and Merz,²²⁰ have studied methods of controlling *Staph. aureus* and *S. enteritidis* by various methods. Although ultraviolet light (2000 to 2950 angstrom units) effective-

duces the count of both organisms in the air and on smooth surfaces, it does not penetrate the surface of custard products; similarly, ozone has proved to be ineffective. Both methods produce an unpleasant odor after the prolonged exposure of custard filled pastry. The growth of both organisms is effectively inhibited by the pH and the type of acid or other substances (lemon, orange, pineapple, apricot and strawberry) present in pure fruit fillings, if prepared by a special formula.²²² The addition of milk, which may act as a buffer to a fruit filling, reduces the inhibitory action. If lemon juice and grated lemon rind is added to a standard custard, there is no inhibition of growth until the concentration becomes so high that the product is unsatisfactory.

Natural chocolate and natural cocoa fillings prepared by a special formula, preferably without eggs, have an inhibiting action on the growth of *Staph. aureus*.²²² This effect seems to be due to the pH and to a combination of substances present in the nonfat part of chocolate and cocoa. Merely bringing custards to a second boil after the addition of the thickening mix renders them sterile to both *Staph. aureus* and *S. enteritidis*.

The utilization of special filling formulas, the proper sanitary handling of products, the boiling of custard or the rebaking of pastry, and the rapid utilization of the product should effectively decrease the number of food-borne outbreaks due to cream-filled and custard-filled pastries.

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and the placing of women in industry. Increasing difficulties are being encountered in restaurants; the lack of responsible personnel trained in the sanitary and proper handling of food, the overburdening of kitchen facilities, the unavailability of proper equipment and in some cases short cuts and improper methods in food processing are the principal causes of the increase in food-borne disease.

Municipal health departments are the chief agents responsible for the sanitation of food establishments. As Korff²⁰² explains, the primary objective of food-establishment inspection is the prevention of food poisoning and infections transmitted by foods. This entails the co-operation of the entire food industry. Training of commercial food handlers is an accepted method of developing safe and sanitary procedures in restaurants and other food-handling establishments. Many municipalities have developed such courses. In Texas²⁰³ the state has assumed this responsibility by means of itinerant instructors, and is convinced that the training is effective in improving the sanitation of establishments.

The perennial question of routine examination of food handlers always appears. In New York City, the finding of each typhoid-fever carrier by routine stool cultures of food handlers cost the city \$50,000; therefore, the examination of food handlers was discontinued in 1934.²⁰⁴ Fort Worth undertook routine examinations of food handlers, and expended \$353.77 for finding each typhoid-fever carrier.²⁰⁵ The local medical society finally concluded that it did not favor routine medical examinations of food handlers—the same conclusion that was reached in San Francisco. Most health authorities have now given up the idea of routine examinations of food handlers as impractical, and as involving an unjustifiable expense of funds that could be utilized for more effective methods of food control.

An important person in the control of food-borne disease is the consumer. The buyer must be aware of what sanitary and insanitary food handling means in relation to health.²⁰⁶ The health authorities must arouse in consumers a desire to trade in shops where food is handled in a clean and sanitary manner. Public opinion is a powerful influence on the commercial food handler; the storekeeper will sell the buyer whatever he demands. When the public is taught to demand safe, clean and sanitary food, properly processed and handled, food-borne disease will be reduced to a minimum.

The elimination of unhealthy animals is one of the veterinary's contributions to the control

of these diseases. McKim²⁰⁷ lists forty-six causes for which meat may be rejected or condemned as unfit for human consumption. The public-health engineer or inspector can do much to track down the mode whereby food may have become infected during processing, and take necessary measures to prevent a repetition.²⁰⁸ Fuchs,²⁰⁹ senior sanitary engineer of the United States Public Health Service, outlines the needs of adequate restaurant sanitation and discusses the provisions of a recommended ordinance regulating food and drink establishments.²¹⁰ This ordinance, or regulations based on it, has been legally adopted in seventy-four counties and by one hundred and twenty-three municipalities in nineteen states. These regulations provide minimum standards for the operation of a licensed or graded food-handling establishment. Inspection of all restaurants is required at least once every six months. If violations of regulations are not corrected after notice in a reasonable time, temporary suspension of the license or degrading (publicly displayed) and, if necessary, hearings, court action and fines are the methods of enforcement.

Horwood and Pesare²¹¹ made sanitary surveys of public eating places in Rhode Island and concluded that ignorance of accepted sanitary requirements and procedures as manifested by the managers and employees of public eating and drinking establishments is the most important single cause of insanitary practices in such places. The development of accepted sanitary procedures has been a concern of the Engineering Section Committee of the American Public Health Association, which publishes periodical reports on sanitary procedures, including standards for disinfection of dishes and utensils, evaluation of dishwashing machines, detergents and other aspects of food sanitation.²¹²

Regulations applying to food-handling establishments must, as Tiedeman²¹³ points out, be reasonable and practical, and must be enforced simultaneously with the education of the food handlers. In the hand-washing of dishes, temperatures of 120°F. for the wash water and 170°F. for the rinse water, thermostatically maintained, are considered adequate. Enough detergent must be used to remove properly all types of materials, in a short time. Soap, alkali, phosphates, silicates and sulfated alcohols are some of the detergents evaluated by Gilcreas and O'Brien.²¹⁴ Alkyl-dimethyl-benzyl ammonium chloride is recommended by Krog and Marshall²¹⁵ as an efficient sanitizing agent for the cleaning of eating and drinking utensils.

The Food and Nutrition Section of the Amer-

ican Public Health Association²¹⁶ surveyed ten public eating establishments to study the effect of an educational program and to evaluate methods. Mechanical washing of drinking glasses and eating utensils is better than hand washing because standards are more easily set, the temperatures of the wash water and the rinse water are higher, and the procedure is more easily controlled. If proper procedures in the hand-washing of dishes are used and clean towels are available, the number of bacteria per utensil can be reduced.

One of the most effective methods of reducing food-borne disease is the enforcement of proper personal-hygiene practices by all food handlers. Strict enforcement of hand washing before handling food, and especially after visiting the toilet, will do much to reduce typhoid fever, *Salmonella* and *Shigella* infections. These diseases are usually spread from the food handler's fingers that have been soiled by his excreta. Keeping the hands away from the mouth and nose and covering the mouth while coughing or sneezing, followed by washing the hands, covering foods whenever possible, refrigerating those that are perishable, reducing the interval between cooking and eating, eliminating food handlers with purulent wounds, boils or infections of the hands, preventing food handlers with sore throats from preparing food—all these will reduce most of the chances of contamination.

Since custard-filled and cream-filled pastries are one of the commonest vehicles for the transmission of food-borne disease, much research has been carried on in an endeavor to make these favorite items of the American diet safe for the consumer. One of the methods for controlling the ubiquitous staphylococcus in such pastries is rebaking, as described by Stritar, Jungewaelter and Dack.²¹⁷ Fifteen bakeries in Baltimore are described by Korff²¹⁸ as using this procedure and finding it satisfactory. Gilcreas and Coleman²¹⁹ state that rebaking for fifteen minutes at 216 to 220°C. (420 to 428°F.) destroys staphylococci and has no effect on the palatability or appearance of the pastry. These authors recommend that larger pastries be rebaked for twenty minutes. There seems to be no doubt that rebaking pastry will effectively eliminate a large proportion of food-borne disease, for which pastry has always been a common vehicle. Staphylococci and *Salmonella* organisms, the two bacteria most frequently found, will thereby be destroyed.

Cathcart, Ryberg and Merz,²²⁰ have studied methods of controlling *Staph. aureus* and *S. enteritidis* by various methods. Although ultraviolet light (2000 to 2950 angstrom units) effectively re-

duces the count of both organisms in the air and on smooth surfaces, it does not penetrate the surface of custard products; similarly, ozone has proved to be ineffective. Both methods produce an unpleasant odor after the prolonged exposure of custard-filled pastry. The growth of both organisms is effectively inhibited by the pH and the type of acid or other substances (lemon, orange, pineapple, apricot and strawberry) present in pure fruit fillings, if prepared by a special formula.²²² The addition of milk, which may act as a buffer to a fruit filling, reduces the inhibitory action. If lemon juice and grated lemon rind is added to a standard custard, there is no inhibition of growth until the concentration becomes so high that the product is unsatisfactory.

Natural chocolate and natural cocoa fillings prepared by a special formula, preferably without eggs, have an inhibiting action on the growth of *Staph. aureus*.²²² This effect seems to be due to the pH and to a combination of substances present in the nonfat part of chocolate and cocoa. Merely bringing custards to a second boil after the addition of the thickening mix renders them sterile to both *Staph. aureus* and *S. enteritidis*.

The utilization of special filling formulas, the proper sanitary handling of products, the boiling of custard or the rebaking of pastry, and the rapid utilization of the product should effectively decrease the number of food-borne outbreaks due to cream-filled and custard-filled pastries.

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of the great toe. There is a mistake in the record, because there is no evidence of calcification in the soft tissue.

DR. BENNETT: May I ask about the type of destruction in the metatarsal bone? Am I correct in thinking that this is not the usual type of destruction that one sees in a neoplasm growing from within a bone? It looks more like atrophy or lysis of the bone rather than the type of destruction that occurs with an invading neoplasm.

DR. SCHATZKI: The defect in the distal end of the first metatarsal looks like a pressure defect rather than one produced by invasion.

DR. TRACY B. MALLORY: This colored picture of the boy's foot is a little dark, but you can see the deep-purplish swelling of the great toe.

DR. BENNETT: The appearance of the swelling and the x-ray changes indicate an unusual lesion. The color and the fluctuant character of the tumor suggest that it contained fluid and, in a hemophilic one thinks of an extravasation of blood. If this lesion were not in a hemophilic, the size and duration of the lesion would certainly suggest a rapidly growing neoplasm. It seems to me, therefore, that we must consider the possibility of a neoplasm whose rapid increase in size may have been due to hemorrhage. An alternative possibility is hemorrhage into the joint, with destruction of the adjacent bones because of pressure. The statement that this was a painless and nontender lesion suggests to me that there may have been some underlying lesion of which we have not been informed. If a neurologic examination was made, I wonder whether the findings were pertinent.

DR. MALLORY: No specific neurologic examination was made.

DR. BENNETT: The reason I ask is that there is a story of marked atrophy in the muscles of this leg and of a pressure sore over the ankle. I also note that the lesion itself was painless and nontender despite the extensive involvement.

DR. ROBERT KAISER: The abstract is incorrect, inasmuch as the mass was painful. The weight of the foot hanging down was painful, and it had to be supported with a cast.

DR. BENNETT: To explain this lesion on the basis of hematoma is difficult. That so much bone could have been destroyed because of pressure is scarcely believable. The size of the lesion and its general appearance suggest tumor as the underlying lesion. As my first choice I suggest that the underlying lesion was a neoplasm, but in order to explain the other changes, it must have been an unusual type of tumor, possibly beginning in the metatarsal articulation. One possibility is a synovial tumor, a

synovioma. Such a tumor has a tendency to grow rapidly, and in a hemophilic, it might enlarge extremely rapidly because of hemorrhage. The only other tumor that I should consider seriously is a destructive type of osteogenic sarcoma. The commonest tumor in this location is a *chondroma*, benign and slowly growing. Such a tumor should have been confined to a single bone rather than spreading across the joint line. My second choice is a *hemarthrosis* that had caused a marked degree of bone destruction through pressure atrophy.

DR. J. H. MEANS: What happened to the knee?

DR. MALLORY: I imagine that attention simply became directed toward something else. What do you think about the diagnosis, Dr. Means?

DR. MEANS: I think it could be explained on the basis of hemophilic arthritis. There is a marked degree of bone atrophy, and a good deal of destruction of the joint surfaces, both of which, to me, are entirely consistent with hemophilic arthritis.

CLINICAL DIAGNOSIS

Hemophilic hemarthrosis?

Malignant tumor of great toe?

DR. BENNETT'S DIAGNOSIS

Malignant tumor of great toe (synovioma or osteogenic sarcoma)?

Hemophilic hemarthrosis, with unusual degree of bone destruction?

ANATOMICAL DIAGNOSIS

Hemophilic hemarthrosis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: It was believed on the ward that this was a desperate situation. A neoplasm could not be ruled out on clinical grounds; in fact, it might well have been present. There appeared to be no possibility of the patient's recovering the use of his foot in any case. Although no one had any great enthusiasm for operating on a boy with an extremely prolonged clotting time, it was believed that amputation should be done. He was given a series of transfusions in rapid succession, which brought the clotting time down to 30 minutes. Amputation was done through the ankle joint, and to everyone's surprise, I take it, there was no particular difficulty or great degree of bleeding.

The resected specimen showed a massive hemorrhage into the joint and surrounding tissues, with varying degrees of organization but no tumor. All the process was evidently hemophilic.

For several days following the operation the patient was mentally confused, which suggested the

Examination of the blood showed a red-cell count of 3,370,000, with a hemoglobin of 65 per cent, and a white-cell count of 6800. The bleeding time was $2\frac{1}{2}$ minutes, and the clotting time $6\frac{1}{2}$ hours.

X-ray examination showed an extremely unusual soft-tissue swelling in the region of the left great toe, 11 cm. in length and 7 cm. in width, which displaced the terminal phalanx of the great toe



FIGURE 2. Roentgenogram of Foot.

forward and had destroyed the entire proximal phalanx and a part of the metatarsal bone (Fig. 2). Periosteal new-bone formation was seen along the remaining portion of the first metatarsal bone. There was definite evidence of external pressure on the second metatarsal bone, which was spread away from the first toe. Flecky calcification was present within the large soft-tissue mass. Examination of the chest was negative.

The patient was given numerous transfusions for the following two months until the clotting time remained at about 30 minutes; an operation was then performed.

DIFFERENTIAL DIAGNOSIS

DR. GRANVILLE A. BENNETT*: We have the story

*Professor of pathology and bacteriology, Tulane University of Louisiana School of Medicine.

of a boy who is said to have been a hemophiliac. I presume that we can accept that diagnosis despite the negative family history. There is no history of repeated or prolonged bleeding unless we assume that the previous joint manifestations were caused by intra-articular hemorrhages. The coagulation time was prolonged. Obvious swelling of one joint following injury and the story of rapidly occurring articular swellings at previous times seem to me to be perfectly consistent with the picture of hemophilia. The joints that were involved are the ones most likely to be affected in this disease.

It is stated in the history that the leg was straightened under anesthesia in a community hospital. This procedure is considered hazardous and likely to cause additional intra-articular injury with more extensive hemorrhage. Manipulations, if carried out at all, should be of a most conservative type.

May we see the x-ray films taken on the first admission?

DR. RICHARD SCHATZKI: This is apparently the only film of the knee. It was taken when the knee was flexed in a cast. Because of the flexion one cannot judge the size of the joint space, but there is irregular destruction of the joint surfaces, in addition to marked decalcification of all the bones that appear in the film.

DR. BENNETT: Do you pay any attention to that area just above the epiphyseal line? Might that be a fracture?

DR. SCHATZKI: It is difficult to tell because the bone is decalcified and there is a cast on top of it. I think it is possible that there was a fracture on one side. I do not believe that it went all the way through.

DR. BENNETT: It seems to me that this x-ray picture is entirely consistent with hemophilic arthritis. The changes are caused by repeated intra-articular hemorrhages, followed by organization of blood clots and invasion of the cartilage by granulation tissue.

Ten months after discharge the boy returned with a large, baseball-sized, bluish-red, somewhat fluctuant tumor in the left great toe. It is stated that the tumor enlarged to the size of a golf ball, and then practically disappeared. These fluctuations in size suggest that the material responsible for the swelling was absorbable, most likely blood.

May we see the x-ray films of the foot?

DR. SCHATZKI: Here is the soft-tissue mass, with complete destruction of the proximal phalanx and partial destruction of the metatarsal. Here you see the tremendous displacement of the distal end

Examination of the blood revealed a red-cell count of 3,240,000 and a white-cell count of 9850. The sedimentation rates were 7, 38, 46 and 50 mm. in fifteen, thirty, forty-five and sixty minutes respectively.

An operation was performed several hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. JOE V. MEIGS: When I read this history the first thing I thought of was an abortion with moderate infection. There is nothing about the patient's temperature until the latter part of the history, when we find that she did have slight fever. The vaginal discharge is probably irrelevant. She may have had a trichomonas infection or endocervicitis; but I do not believe it is important. The abdominal cramps radiating down the thighs also suggest an abortion. Because of the early right-sided pain, cellulitis on the right side should be considered.

Regular intermenstrual pain is not unusual at the time of ovulation. The patient had been married four and a half years and had never been pregnant, but the possibility is always present.

The cervix was large, patulous, soft, ragged and bleeding. That could have been because the patient was pregnant or because she had been recently operated on, with cauterization of the cervix. The fact that the uterus was small makes one wonder whether, if she were pregnant, the pregnancy was outside the uterus.

The white-cell count is not consistent with infection. The urine was probably not a catheter specimen, hence the cells in the sediment are unimportant. Infection of the cervix or uterus was apparently suspected because cultures were taken, which were negative for a beta-hemolytic streptococcus.

Without curettage the patient quieted down and there was no need to do anything further. No dates are given, but the history indicates that she was going through normal periods before the second admission. I should like to learn whether the endometrial biopsy showed any evidence of decidua. Do you know, Dr. Sniffen?

DR. RONALD C. SNIFFEN: It did not.

DR. MEIGS: The story at the time of re-entry makes one think of the interruption of an early uterine pregnancy—possibly by means of the endometrial biopsy—or of an extrauterine pregnancy.

One must consider whether she had acute appendicitis, but that does not seem to fit in with

the picture. The white-cell count was too low for a serious infection.

The fact that operation was performed several hours after admission certainly makes me think of an acute abdominal lesion, such as a twisted ovarian cyst or an extrauterine pregnancy, or that she was bleeding sufficiently to make the gynecologist believe that she ought to be curetted.

Was a Friedman test done?

DR. BENJAMIN CASTLEMAN: No.

DR. MEIGS: I am unable to make a clear-cut diagnosis, but I believe that the patient had either an incomplete abortion with moderate infection in the uterus and pelvis, a twisted ovarian cyst or an extrauterine pregnancy. She had an infection, and the first entry was probably for an abortion, and the subsequent one for an extrauterine pregnancy, that being why she was operated on.

DR. FRED SIMMONS: We were not at all sure what this patient had, although our preoperative diagnosis was ectopic pregnancy. She was seen in consultation with an obstetrician, who agreed with our tentative diagnosis and thought that exploration was indicated. At operation the pelvis was found to be extensively involved with endometriosis. The right tube and ovary were involved in a dense mass of adhesions, which included the appendix. The appendix was of normal size, definitely red, indurated, and kinked and was covered with fibrin at the site of the kink, which was suggestive of acute appendicitis. Because the patient was very anxious to have children we were conservative. The appendix was dissected away from the tubo-ovarian mass with some difficulty and only a portion of the right ovary was resected. The left adnexa appeared normal and were left intact. There was no ectopic pregnancy.

DR. MEIGS: I think my reasoning would be just the same now that I know I was wrong. I certainly thought of appendicitis but I see no reason why I should have concluded that she had it.

CLINICAL DIAGNOSIS

Extrauterine pregnancy?
Tubo-ovarian abscess?
Twisted ovarian cyst?

DR. MEIGS'S DIAGNOSES

Extrauterine pregnancy?
Early abortion?
Twisted ovarian cyst?
Pelvic infection.

ANATOMICAL DIAGNOSES

Acute appendicitis.
Endometriosis of appendix and right ovary.

possibility of subarachnoid or cerebral bleeding. Again, no one was enthusiastic about doing a lumbar puncture, and since after about a week it showed signs of spontaneously clearing up, the central nervous system was left uninvestigated. To everybody's surprise and relief, it was possible to get the boy out of the hospital.

CASE 29252

PRESENTATION OF CASE

First admission. A twenty-seven-year-old housewife entered the hospital because of vaginal bleeding and cramps of four days' duration.

During the seven years prior to admission the patient noted an intermenstrual vaginal discharge that was foul smelling, white or yellow, and at times required a pad. She often had low back pain. Twelve days prior to admission she entered a community hospital where dilatation and curettage revealed a "hypertrophied lining"; a "cervical polyp" was cauterized. Following this she had a slight, "pink" vaginal discharge until four days prior to admission when she began to flow profusely. Two days prior to admission she developed severe lower abdominal cramps most marked on the right and occasionally radiating down the front of the thighs. She passed large blood clots and required pads every one and a half hours during the next two days.

The menarche occurred at thirteen years, the periods were regular, with an interval of twenty-five to twenty-nine days, and each lasted four to seven days. During the first three days abdominal cramps were severe and frequently required bed rest. The patient occasionally had intermenstrual bleeding not associated with pain; this occurred about two weeks after menstruation, lasted one day and required a pad. The last normal menstrual period began twenty-three days prior to admission. She had been married four and a half years but no pregnancies had occurred, although no precautions had been taken.

The family and past histories were not remarkable.

Physical examination revealed a well-developed and well-nourished woman. The heart, lungs and abdomen were normal. There was profuse uterine bleeding. The cervix was large, patulous, soft, ragged and bleeding. The uterus was small, slightly tender and pointed anteriorly; the vaults were negative.

The blood pressure was 126 systolic, 72 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 3,780,000 with a hemoglobin of 11.6 gm. and a white-cell count of 8400, with 68 per cent neutrophils. The sedimentation rates were 4, 16, 27 and 38 mm. in fifteen, thirty, forty-five and sixty minutes respectively. The urine gave a + test for albumin, and the sediment contained many red cells, 15 to 20 white cells and an occasional epithelial cell per high-power field. Cervical cultures were negative for beta-hemolytic streptococci.

The temperature gradually rose after admission and reached 101°F. on the third hospital day. She was treated with sulfadiazine by mouth, and the temperature promptly became normal. Vaginal packs controlled the bleeding, and the patient was discharged somewhat improved on the ninth hospital day.

Second admission (seven months later). Following her previous entry she stained for five to sixteen days before her expected periods and frequently had an intermenstrual creamy vaginal discharge. About six weeks before re-entry her physician started a routine sterility investigation, and about one month later insufflation of the tubes and an endometrial biopsy were performed. The latter showed proliferative endometrium. Nine days before re-entry another endometrial biopsy revealed secretory endometrium. Two days later she started to flow, although this was only the twenty-fourth day since the beginning of the previous menstrual period. During the week prior to admission the temperature varied from 100 to 101.4°F. and she had crampy pain in the lower abdomen and nausea but no vomiting. Bleeding was profuse and required fifteen to twenty pads a day. During the six days prior to admission she was forced to go to bed. She was slightly constipated. There were no urinary symptoms or chills.

Physical examination disclosed a pale, slightly apprehensive woman who was perspiring freely. The heart and lungs were normal. The abdomen was slightly distended and diffusely tender, with the chief locus of tenderness over the right lower quadrant, where a mass could be made out. One examiner demonstrated rebound tenderness, particularly in the right lower quadrant. Rectal examination revealed a fusiform mass in the right vault, a large patulous cervix that seemed softer than normal and a uterus that was larger than normal. The pelvic examination confirmed these findings, and fresh and clotted blood was found in the vagina.

The blood pressure was 110 systolic, 65 diastolic. The temperature was 100°F., the pulse 120, and the respirations 28.

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"MASTERY OF THE AIR"

THE course of the present war has illustrated the importance of "mastery of the air" in gaining victory over our enemies in combat. Other almost equally important enemies behind the battle lines and on the home front, which are responsible for many deaths and casualties in wartime and which must be conquered, are epidemics of respiratory infections. Although the final victory over the latter enemies is still far off, the weapons are now being forged that may lead to this victory. Some of these weapons are concerned with the attempt to gain mastery of the air by controlling its content of disease-producing viruses and bacteria. This, it is hoped, will reduce or eliminate the so-called "air-borne infections," which include not

only those of the respiratory tract but also certain types of wound infections.

During World War I extensive studies were carried out, particularly in army hospitals, on the mode of spread of respiratory and wound infections. At that time the importance of air-borne infectious agents was recognized. Since the chief offending organism at that time was the hemolytic streptococcus and since the most important mode of spread was by way of the human respiratory tract, some attempts were made to control such infections in hospital wards. These methods involved general cleanliness, proper spacing, screening and the masking of patients and personnel.¹

The opinion is now widely held that respiratory infections are spread through the air directly by droplets laden with organisms that are expelled from the infected respiratory tract and by droplet nuclei, which are minute particles resulting from the evaporation of the relatively large droplets. These nuclei bear virulent organisms but they are small enough and light enough to remain suspended in the air for considerable periods, during which they may be inspired by other persons and thus produce spread of the disease. Direct infection of contacts may, of course, take place by means of droplet infection. Turner, Jennison and Edger-ton,² of the Massachusetts Institute of Technology, have made extensive studies of such droplets as they are expelled during coughing and sneezing. By means of specially perfected high speed photography utilizing strong indirect illumination, they have been able to visualize these droplets and have shown that tremendous numbers are expelled during the act of sneezing and that smaller, yet considerable, numbers are ejected by coughing and speaking. Many of the large particles tend to fall rather rapidly, but in a significant number, evaporation takes place rapidly and results in small particles that may serve as germ-carrying droplet nuclei. Their studies emphasize the importance of controlling the spread of the droplets during sneezing, especially by persons suffering from the acute stage of a common cold. Most of the common respiratory pathogens have been recovered from the air, particularly in

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The appendix was covered with fibrin, and on microscopic examination, in addition to the acute infection of the serosa and muscularis, there was extensive endometriosis throughout the serosa. The ovary also showed endometriosis. Dilatation and curettage, which were also performed, showed that the endometrium was in the secretory phase, without any suggestion of decidua.

DR. SIMMONS: We debated whether to do the dilatation and curettage before laparotomy but decided not to because we thought we had to explore in any event. After exploration we still could not explain the profuse uterine bleeding and therefore did the dilatation and curettage.

DR. CASTLEMAN: Do you think, Dr. Meigs, that the abnormal bleeding could have been due to the diffuse endometriosis throughout the pelvis?

DR. MEIGS: This patient had marked endometriosis, but one does not see many patients with endometriosis with bleeding as severe as this. I could not make that diagnosis.

DR. SIMMONS: The patient made an uneventful convalescence, and the subsequent periods have been normal.

DR. JOSEPH AUB: What about the leukorrhea?

DR. SIMMONS: No trichomonas were found, and cultures of the cervix were negative. I think that leukorrhea can occur on a nervous basis, and perhaps this patient falls into that class.

DR. MEIGS: I have seen flare-ups of pelvic inflammation in patients who have had insufflation of the tubes and endometrial biopsy. Following

any manipulation in the endometrial cavity one occasionally sees moderate intrapelvic inflammatory disease. It is rare, of course, but this might have been responsible for the second flare-up.

DR. JOHN ROCK: Do you not suppose the mucoid disturbance was due to a hyperactive cervix? If it was mucoid, it must have come from the cervix, not the vagina; if purulent, it must have meant endocervicitis. We naturally expect to be able to see an endocervicitis that causes profuse leukorrhea. Probably the only way to cure such a patient is to cauterize the cervix, thus getting rid of the hyperactive mucous glands. If that does not result in cure, a repeated series of sulfa drugs sometimes clears up what is left. I have seen cases of profuse leukorrhea in which the cervixes were apparently normal; however, the deeper glands of the cervix were chronically infected and hyperactive.

DR. MEIGS: Was not the sedimentation rate rapid, Dr. Beckman?

DR. WILLIAM BECKMAN: Yes.

DR. MEIGS: That is one of the differential diagnostic points we raise between appendicitis and acute salpingitis. In cases of salpingitis the sedimentation rate is usually rapid, whereas in cases in which the appendix is ruptured it is not. Here is one case of appendicitis in which the sedimentation was rapid.

DR. FRANCIS INGERSOLL: In the Emergency Ward, we formerly used the sedimentation rate to differentiate salpingitis and appendicitis, but when Dr. Roy Cohn carefully checked these cases, he found many cases of appendicitis with rapid sedimentation rates.

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Most of the common respiratory pathogens have been recovered from the air, particularly in

hospital wards where infected persons are being nursed or where there are large congregations of persons.³ The numbers of such bacteria that are recovered during epidemics of respiratory infections are large and significant, and the possibility of spread of air-borne infections has acquired great significance because of the concentration of persons in places of amusement or other indoor assemblies, in industrial plants, in military barracks, on ships, in hospital wards and in air-raid shelters.

The earlier methods of studying the number of pathogenic bacteria found in the air involved exposing plates containing suitable culture mediums in various strategic locations and counting the number of colonies after these plates had been exposed for a desired period and properly incubated. Other methods and apparatus for obtaining samples of air and subjecting them to bacterial counts have been devised, the most elaborate of which is the Wells centrifuge. The later methods offer a better means of evaluating the number of bacteria suspended in the air in contrast to those that sediment onto the surface of exposed culture plates. All these procedures have been used in the evaluation of newer methods that are designed to reduce or eliminate infection of the air.⁴

Wells and his co-workers⁵ have been interested in the utilization of ultraviolet radiation as a means of reducing or eliminating air-borne infection in enclosed areas. The studies made by Hart⁶ at Duke Hospital offer fairly convincing evidence that ultraviolet radiation may bring about a considerable reduction in wound infections following surgical operations. In hospital wards, particularly those for children with communicable diseases, lamps have been installed to produce a barrier of ultraviolet light through which air and its contents pass from the potentially infected atmosphere of the infected patient's cubicle into the rest of the ward.⁷ In this manner some evidence has been gathered to suggest that the incidence of cross infections, even of such a highly contagious disease as chicken pox, can be markedly reduced. The enthusiasm of some of the workers in this

field, however, is not universally shared by other observers. Objections have been raised both to the interpretation of the results and on the grounds of the difficulties involved in properly equipping and maintaining the necessary apparatus, as well as in protecting patients and staff from the untoward effects of overexposure. These objections have deterred the majority from adopting this method of control. Thus far there have been no large-scale studies in which ultraviolet radiation was employed, or if they have been made, the results are not available to permit an evaluation of its practicability.

A second method of control of air-borne infections involves chemical disinfection of the air. Most disinfectants that in the past have been found effective in killing bacteria in the atmosphere have not proved useful because of certain undesirable properties, particularly their high toxicity when inhaled in the concentrations necessary to produce the desired result. Investigations carried out over a number of years by Trillat⁸ in France, then more recently by British workers,⁹ and in the past few years by Robertson and his co-workers¹⁰ in Chicago have resulted in the discovery of certain aerosols that, when sprayed or vaporized, are highly effective in rapidly disinfecting the atmosphere. Propylene glycol is one of the substances that has been tried extensively, and Robertson and his co-workers have found it to be the most effective and the least toxic. This substance in a concentration of one part in two to four million produces rapid sterilization of air containing fairly large numbers of the common pathogenic bacteria, and is also effective in destroying virulent influenza virus. Even in a dilution as high as one part in fifty million, it is able to reduce to a considerable extent the number of bacteria. Since more concentrated amounts of this substance can apparently be inhaled by animals for long periods without deleterious effects, its toxicity is low. Furthermore, bactericidal concentrations can readily be obtained by simple means involving either mechanical spraying or evaporation at suitable temperatures. The mechanism by which these substances operate appar-

ently involves a coating of the droplet nuclei by the aerosol, which condenses on the surface and results in death of the bacteria.

Many problems remain to be solved, and extensive studies are being carried out in an attempt to work out the details of this method and its applicability. It must be ascertained to what extent the materials, in the concentrations in which they must be used, are inflammable or explosive, whether or not they are toxic when inhaled in these concentrations for long periods; and what is the effect of variations in temperature and humidity. Up to the present time their use, too, has not been tested on a large scale and under conditions of crowding and mass infection, such as are likely to prevail on troopships, in air-raid shelters or in other similar situations, particularly during the course of epidemics of respiratory infections. Further studies with aerosols and with other germicidal substances are being carried out both in this country and in Great Britain.

A third factor of importance in the spread of respiratory infections and in the contamination of wounds in operating rooms or hospital wards is related to dust. Experiments carried out in England have shown that the number of pathogenic bacteria that can be recovered from the air in a hospital ward varies markedly in different parts of the day.¹¹ The largest numbers are found in the morning hours during and after the time when the beds are made and the wards are cleaned. These counts correlate directly with the counts of the numbers of dust particles. Furthermore, numerous studies in the past have shown that the dust of rooms in which patients with respiratory infections are nursed contains large numbers of virulent bacteria similar to those found in the patients. Control of dust is, therefore, another significant factor in the reduction of air-borne infection. The British studies have led to specific recommendations for this purpose. These involve the avoidance of dry dusting and the substitution of wet mopping, which in turn involves the use of suitable flooring material for this purpose. More

specifically, the use of liquid paraffin films has been recommended for floors and for blankets, bedspreads and other linen articles that contribute to the dust of the sick room. When treatment with liquid paraffin or other suitable oils is properly carried out, an invisible surface film is produced that apparently does not have much effect on the appearance of the flooring and linens and does not alter their properties, but, nevertheless, does materially reduce the amount of dust that is raised during the bed making and the ward-cleaning periods. A parallel reduction in the bacterial count of the air is observed following this procedure.

None of these methods are effective in eliminating the direct spread of infection from droplets sprayed by individuals with acute respiratory infections during coughing and sneezing. Such droplets contain highly virulent agents in high concentration. The principles involved in the conception of "isolation" and "barrier nursing" are still important to bear in mind and to practice if a reduction in the spread of droplet or contact infection is to be attained.

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ANDREAS VESALIUS

FOUR hundred years ago this month—June, 1543—a simple yet singular event occurred that has served as a landmark both in the procedure and in the conveyance of scientific thought. This event was the publication of the epoch-making book by Andreas Vesalius entitled *De Humani Corporis Fabrica*. It is most fitting to take cognizance of the quadricentennial of this publication. For the first time in the history of anatomy the fabric of the human body was represented as of and on this earth. Prior to the time of Vesalius, books were written on what might be called the idealized man. Vesalius, however, learned about the imperfections in the structure of the body from many firsthand observations and boldly set down these observations in his text. A distinguishing mark of this work is the fact that he alone carried out the dissections and demonstrations. This method was in striking contrast to earlier periods when dissections were performed either by a famulus, a demonstrator or an instructor. It is also important to note that Vesalius introduced the regular use of a mounted skeleton and other preparations to make clear his lectures. The Renaissance it may be recalled looked upon Man as a whole and upon Nature as essentially friendly. This point of view was vividly expressed in the *Fabrica*.

Vesalius was born in Brussels in 1514, five years before the death of Leonardo da Vinci. After pursuing studies at Louvain, Leyden and Paris, he received the coveted appointment as professor of surgery and anatomy at the great Italian university at Padua, the *mater gloriosa studiorum*. This university in particular fostered freedom of thought and leaned quite sympathetically toward those artists whose work began to influence the new scientific outlook.

It should be remembered that Vesalius was an artist as well as a naturalist and a humanist. And so it came about that he encouraged his friend, Stephen van Calcar, a pupil of the celebrated Titian, to make the superb illustrations that accompany the text of the *Fabrica*. This classic book

will always remain the result of the indissoluble union of the scientist and the artist. It was through the efforts of Vesalius and van Calcar that the concepts of Galen, which had hitherto constituted a stable center for formalized and conventionalized medical thought, were almost completely broken down. A new method and spirit arose, which was calculated to lift all science to higher levels. We today may well remember Andreas Vesalius by the following words, which he had printed upon the fine figure of Death in the *Fabrica*:

Vivitur ingenio, caetera mortis sunt

[One lives for the spirit, all else belongs to death].

MEDICAL EPONYM

WEIL-FELIX REACTION

A paper entitled "Zur serologischen Diagnose des Fleckfiebers [Serologic Diagnosis of Typhus Fever]," by E. Weil (1880–1922) and A. Felix (b. 1887), appeared in *Wiener klinische Wochenschrift* (29:33–35, 1916). A portion of the translation follows:

During the latter part of September, 1915, we had an opportunity to study bacteriologically, serologically and, in part, clinically, a group of cases of typhus fever in the town of R., in East Galicia. . . . Because of the coincident prevalence of typhoid fever, we were in doubt concerning the diagnosis in the first of our cases. . . . Nevertheless we were struck by the fact that no typhoid bacilli could be recovered from any of the first nine cases observed. . . . On the other hand we cultivated a micro-organism from the urine of patient V. . . . that was not agglutinated by typhoid, paratyphoid A and B or dysentery anti-serums, but which did show agglutination with the patient's own serum in a 1:200 dilution. . . . Thirty-three cases observed in R. had been diagnosed as typhus fever. . . . All thirty-three serums gave an agglutination reaction with the bacillus under cultivation. . . . The specific agglutinins appeared at an early stage of the illness. They had reached their maximum at the time of appearance of the exanthem, persisted at this level during the febrile period of approximately fourteen days and quickly disappeared after defervescence. . . .

We do not feel justified in regarding this germ as the provocative agent of typhus fever. . . . Nevertheless we apparently have in this micro-organism a means of assistance in the diagnosis of typhus fever.

The organism is further described as a "short, delicate gram-negative rod, resembling proteus, and weakly motile."

R. W. B.

